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     FILE 'USPATFULL, CAPLUS, EMBASE' ENTERED AT 12:38:35 ON 28 AUG 2003
L1          1887 FILE USPATFULL
L2         18346 FILE CAPLUS
L3         10024 FILE EMBASE
     TOTAL FOR ALL FILES
L4         30257 S GENISTEIN OR QUERCETIN

     FILE 'USPATFULL, CAPLUS, EMBASE' ENTERED AT 12:38:41 ON 28 AUG 2003
L5          1529 FILE USPATFULL
L6            99 FILE CAPLUS
L7           477 FILE EMBASE
     TOTAL FOR ALL FILES
L8          2105 S ACNE AND SCAR?
L9            38 FILE USPATFULL
L10            0 FILE CAPLUS
L11            0 FILE EMBASE
     TOTAL FOR ALL FILES
L12           38 S L4 AND L8
L13        16319 FILE USPATFULL
L14         6076 FILE CAPLUS
L15        25875 FILE EMBASE
     TOTAL FOR ALL FILES
L16        48270 S SCAR OR SCARRING OR CICATRIZATIONC
L17        16579 FILE USPATFULL
L18         6279 FILE CAPLUS
L19        26162 FILE EMBASE
     TOTAL FOR ALL FILES
L20        49020 S SCAR OR SCARRING OR CICATRIZATION
L21            4 FILE USPATFULL
L22            7 FILE CAPLUS
L23            8 FILE EMBASE
     TOTAL FOR ALL FILES
L24           19 S L20 (1S) L4
L25          678 FILE USPATFULL
L26           51 FILE CAPLUS
L27          351 FILE EMBASE
     TOTAL FOR ALL FILES
L28         1080 S L16 (1S) ACNE?
L29           15 FILE USPATFULL
L30            0 FILE CAPLUS
L31            0 FILE EMBASE
     TOTAL FOR ALL FILES
L32           15 S L28 AND L4
                 SAVE ALL LSCARMMP/L
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L12 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1985:481706 CAPLUS
DN 103:81706
TI Prevention and treatment of **scars** with enzymes
IN Pinnell, Sheldon R.
PA Bio-Specifics N. V., Neth.
SO U.S., 4 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K037-48
NCL 424094000
CC 1-12 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4524065	A	19850618	US 1983-520203	19830804
	US 4645668	A	19870224	US 1985-716742	19850327
PRAI	US 1983-520203		19830804		

AB The enzyme **collagenase** [9001-12-1] and the **collagenase** -hyaluronidase mixt. [97726-75-5] were used for the prevention of an for the dissoln. of mammalian cicatrices such as **acne scars**, keloids, and other hypertrophic **scars** in human subjects after intralesional administration.
ST **scar** treatment prevention **collagenase** hyaluronidase
IT Skin, disease or disorder
(**scar**, prevention and treatment of, with **collagenase** and hyaluronidase, in humans)
IT 9001-12-1 97726-75-5
RL: BIOL (Biological study)
(**scars** prevention and treatment with, in humans)

=>

L3 ANSWER 8 OF 10 USPATFULL on STN

SUMM The present invention relates to an anhydrous, stable **retinol**- or vitamin A-based cosmetic or pharmaceutical composition for the skin and to the use thereof for the treatment of skin disorders, in particular for the **treatment** of acne, keratinization or **scarring** problems, light-related aging, and the prevention and softening of wrinkles.

ACCESSION NUMBER:	2000:7069 USPATFULL
TITLE:	Anhydrous stable retinol based cosmetic or pharmaceutical composition
INVENTOR(S):	Segot, Evelyne, Nogent sur Morne, France Laugier, Jean-Pierre, Antony, France
PATENT ASSIGNEE(S):	L'Oreal, Paris, France (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6015568		20000118
APPLICATION INFO.:	US 1996-627480		19960404 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-317879, filed on 4 Oct 1994, now abandoned		

	NUMBER	DATE
PRIORITY INFORMATION:	FR 1993-11850	19931005

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Page, Thurman K.
ASSISTANT EXAMINER:	Berman, Alysia
LEGAL REPRESENTATIVE:	Nixon & Vanderhye P.C.
NUMBER OF CLAIMS:	7

preparation. U.S. Pat. No. 4,847,084 discloses two ointments for treatment of decubitus ulcers, Decubitane #1 and #2, which are based upon a debriding enzyme, fibrinolysin, with additives including chlorophyll and povidoneiodine. U.S. Pat. No. 3,622,668 discloses a **scar**-inhibiting lotion for **treatment** of livestock injuries which contains phenol, **retinol**, ergosterol and olive oil, or fish oil. None of the disclosed or claimed "comfrey" treatment formulations for humans or other mammals are foams, controlled-release particles, controlled-release implants, emulsions, vesicles, liposomes, aerosols or micelles.

ACCESSION NUMBER:	94:62220 USPATFULL
TITLE:	Polyphase fluid extraction process, resulting products and methods of use
INVENTOR(S):	Steuart, Gary M., 98 Viking Terr., Northfield, MN, United States 55057 Huffstutler, Jr., M. Conrad, 6200 Lynn La., Lago Vista, TX, United States 78645

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5330756		19940719
APPLICATION INFO.:	US 1992-980839		19921124 (7)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1990-599616, filed on 18 Oct 1990, now abandoned
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Page, Thurman K.
ASSISTANT EXAMINER:	Azpuru, Carlos
LEGAL REPRESENTATIVE:	Huffstutler, Jr., M. Conrad
NUMBER OF CLAIMS:	5
EXEMPLARY CLAIM:	1
LINE COUNT:	847

L7 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN

IT 117-39-5, **Quercetin** 153-18-4, Rutin 520-26-3, Hesperidin
1340-08-5, Citrin 9004-61-9, Hyaluronic acid 10236-47-2, Naringin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(bioflavonoids for retardation of skin aging)

IT 9001-12-1, **Collagenase** 37326-33-3, Hyaluronoglucosaminidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; bioflavonoids for retardation of skin aging)

ACCESSION NUMBER: 1995:618220 CAPLUS
DOCUMENT NUMBER: 123:17505
TITLE: Bioflavonoids for retardation of skin aging
INVENTOR(S): Backhaus, Erwin
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 2 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4339486	A1	19950524	DE 1993-4339486	19931119

PRIORITY APPLN. INFO.: DE 1993-4339486 19931119

L7 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN

AB Flavones or anthocyanins as matrix metalloprotease inhibitors and their extn. from medicinal plants (e.g. Scutellaris baicalensis roots) for therapeutic use are claimed. Baicalein inhibited the activity of matrix metalloprotease (e.g **collagenase**) with IC50 = 25 .mu.g/mL. The flavones or anthocyanins may be used for treating deformative arthropathy, gingivitis, cancer metastasis, and chronic rheumatism.

IT 90-18-6P, Quercetagetin 117-39-5P, **Quercetin** 134-04-3P, Pelargonidin 480-40-0P, Chrysin 491-67-8P, Baicalein 491-70-3P, Luteolin 520-18-3P, Kaempferol 520-36-5P, Apigenin 528-53-0P, Delphinidin 528-58-5P, Cyanidin 529-44-2P, Myricetin 529-53-3P, Scutellarein 18003-33-3P, 6-Hydroxyluteolin
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(flavones or anthocyanins as matrix metalloprotease inhibitors and their extn. from plants for therapeutic use)

IT 9001-12-1P, **Collagenase** 37259-58-8P, Serine proteinase 81669-70-7P, Metalloprotease 146480-36-6P, Gelatinase B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors; flavones or anthocyanins as matrix metalloprotease inhibitors and their extn. from plants for therapeutic use)

ACCESSION NUMBER: 1996:417847 CAPLUS
DOCUMENT NUMBER: 125:67741
TITLE: Flavones or anthocyanins as matrix metalloprotease inhibitors and their extraction from medicinal plants for therapeutic use
INVENTOR(S): Kumagai, Kazuo; Fujiwara, Fumi; Negoro, Takaatsu; Kaneoka, Shoji; Saji, Kitaro
PATENT ASSIGNEE(S): Sumitomo Pharma, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08104628	A2	19960423	JP 1994-266264	19941004

PRIORITY APPLN. INFO.: JP 1994-266264 19941004
OTHER SOURCE(S): MARPAT 125:67741

side showed a greatly thickened epidermis and an increased number of new blood vessels using the conventional haemotoxylin and eosin technique. A special stain (Hale) showed increased glycosaminoglycans. Van Gieson's stain showed deeper staining of the collagen bundles, reflecting increased synthesis of collagen. Moreover, a moderate inflammatory reaction in the fibrous septaedividing the fat compartments of the subcutaneous tissue was eliminated on the retinoic acid side. Fibrosis (**scarring**) was also **reduced**.

CLM What is claimed is:

1. A method for retarding and reversing cellulite, comprising topically applying to human **skin** a **retinoid** in an amount and for a period of time effective to retard and reverse cellulite, said amount being insufficient to be excessively irritating.

2. The method according to claim 1, wherein the **retinoid** is present in an emollient vehicle.

3. The method according to claim 1, wherein the amount of **retinoid** is an amount equivalent to about 0.01% to about 0.25% **retinoic** acid by weight concentration.

4. The method according to claim 2, wherein the amount of **retinoid** in the emollient vehicle is an amount equivalent to about 0.05% to about 0.1% **retinoic** acid by weight concentration.

5. The method according to claim 1, wherein the **retinoid** is applied in a once daily dosage.

6. The method according to claim 1, wherein the **retinoid** is applied in a twice daily dosage.

7. A method according to claim 1, wherein said **retinoid** is selected from the group consisting of **retinoic** acid, **retinoic** acid derivatives and stereoisomers thereof.

8. A method according to claim 7, wherein said **retinoid** comprises **retinoic** acid.

9. A method of preventing recurrence of cellulite in patients in which the effects of cellulite has been retarded and reversed, comprising topically applying to human **skin** of said patients a **retinoid** in an amount and for an indefinite maintenance period of time effective to prevent cellulite, said amount being insufficient to be excessively irritating.

10. The method according to claim 9, wherein the **retinoid** is present in an emollient vehicle.

11. The method according to claim 9, wherein the amount of **retinoid** is an amount equivalent to about 0.01% to about 0.25% **retinoic** acid by weight concentration.

12. The method according to claim 10, wherein the amount of **retinoid** in the emollient vehicle is an amount equivalent to about 0.05% to about 0.1% **retinoic** acid by weight concentration.

13. A method according to claim 9, wherein said **retinoid** is selected from the group consisting of **retinoic** acid, **retinoic** acid derivatives and stereoisomers thereof.

14. A method according to claim 13, wherein said **retinoid** comprises **retinoic** acid.

L15 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:796565 CAPLUS
DN 128:7221
TI Ointment for prevention of facial **scarring** and blemishes of the face and body
PA Puyravaud, Michelle, Fr.
SO Fr. Demande, 6 pp.
CODEN: FRXXBL
DT Patent
LA French
IC ICM A61K007-48
CC 62-4 (Essential Oils and Cosmetics)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2743720	A1	19970725	FR 1996-754	19960123
	FR 2743720	B1	19980410		
PRAI	FR 1996-754		19960123		

AB An ointment is disclosed for use in prevention of sequelae of **scarring** of the face and for treatment of blemishes of the face and body such as **acne** and mini-cysts. Thus, an ointment is formulated which is comprised (in grams) of washed sulfur 2,5-5.0, salicylic acid 2.0-5.0, and essential oils, including borneol 1.0-3.0, cypress oil 0.100-0.150, geranium essential oil 0.100-0.150, lavender oil 0.100-0.150, grapefruit oil 0.100-0.150, patchouli oil 0.100-0.150, rose oil 0.100-0.150, sassafras oil 0.100-0.150, and ylang-ylang 0.100-0.150.
ST skin ointment **acne scarring** facial blemish
IT Essential oils
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(cypress; ointment for prevention of facial **scarring** and blemishes of the face and body)
IT Head
(face; ointment for prevention of facial **scarring** and blemishes of the face and body)
IT Essential oils
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(geranium; ointment for prevention of facial **scarring** and blemishes of the face and body)
IT Essential oils
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(grapefruit; ointment for prevention of facial **scarring** and blemishes of the face and body)
IT **Acne**
(inhibitors; ointment for prevention of facial **scarring** and blemishes of the face and body)
IT Essential oils
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(lavender; ointment for prevention of facial **scarring** and blemishes of the face and body)
IT Cosmetics
Keloid
Ylang-ylang (Cananga odorata)
(ointment for prevention of facial **scarring** and blemishes of the face and body)
IT Essential oils
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(ointment for prevention of facial **scarring** and blemishes of the face and body)

IT Essential oils
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(patchouli; ointment for prevention of facial **scarring** and blemishes of the face and body)

IT Essential oils
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(rose; ointment for prevention of facial **scarring** and blemishes of the face and body)

IT Essential oils
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(sassafras; ointment for prevention of facial **scarring** and blemishes of the face and body)

IT 507-70-0, Borneol
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(ointment for prevention of facial **scarring** and blemishes of the face and body)

IT 7704-34-9, Sulfur, biological studies
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(washed; ointment for prevention of facial **scarring** and blemishes of the face and body)

keloid

<dermatology> A sharply elevated, irregularly shaped, progressively enlarging scar due to the formation of excessive amounts of collagen in the corium during connective tissue repair.

Origin: Gr. Kel = tumour, eidos = form

(18 Nov 1997)

Previous: Kelly clamp, Kelly, Howard, Kelly's operation, Kelly's rectal speculum
Next: keloidosis, keloplasty, kelosomia, kelotomy, kelp, kelpfish, kelpy

hypertrophic scar

An elevated scar resembling a keloid but which does not spread into surrounding tissues, is rarely painful, and regresses spontaneously; collagen bundles run parallel to the skin surface.

(05 Mar 2000)

Previous: hypertrophic pyloric stenosis, hypertrophic rhinitis, hypertrophic rosacea
Next: hypertrophied, hypertrophied lenticels, hypertrophy

cicatrix

The formation of new tissue in the process of wound healing.

(12 Dec 1998)

Previous: cicatricial horn, cicatricial pemphigoid, cicatricotomy, cicatrisation
Next: cicatrix, hypertrophic, cicatrizant, cicatrization

cicatrization

1. The process of scar formation.

2. The healing of a wound otherwise than by first intention.

(05 Mar 2000)

Previous: cicatricotomy, cicatrisation, cicatrix, cicatrix, hypertrophic, cicatrizant
Next: cicatrization atelectasis, ciclopirox olamine, cicutoxin, cidofovir

SUMM There is increasing interest in introducing vitamins such as vitamins A, B, C, D, E and F (essential fatty acids), as well as other active agents, into cosmetic and/or dermatological compositions with a view to providing specific treatments against, for example, excessive weight, skin aging, dry skin, skin pigmentation, **acne** and certain skin diseases (psoriasis) or, alternatively, in order to promote the cicatrization (**scar** formation) and/or restructuring of the skin.

DETD As a further example, it is possible to use the glucosyl derivative of **quercetin** as a first precursor and a **quercetin** ester such as **quercetin** ferulate as a second precursor, in order to liberate **quercetin** synergistically on application to the skin of a composition containing this pair of precursors.

CLM What is claimed is:

9. The composition of claim 8, wherein said first precursor is a C.sub.3 to C.sub.6 vitamin or **quercetin** monosaccharide, and said second precursor is selected from the group consisting of ascorbic acid phosphates, retinol phosphates, tocopherol nicotinates, retinol palmitates, ascorbic acid palmitates, tocopherol acetates, retinol acetates, ascorbic acid acetates, retinol propionates, ascorbic acid propionates, **quercetin** palmitates, **quercetin** acetates, **quercetin** propionates, **quercetin** ferulates, and mixtures thereof.

23. The composition of claim 22, wherein said skin active agent is selected from the group consisting of vitamin A, vitamin C, vitamin E, lactic acid, **quercetin** and retinol.

PI US 5607921 19970304

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L29 ANSWER 2 OF 5 USPATFULL on STN

DETD [0070] Agents may include, without limitation, the following compositions and derivatives and analogs thereof: hair dyes, vegetable dyes, food coloring, fabric dyes, tissue stains, shoe or leather dyes, other plant products (such as **flavonols**, chlorophyll, copper chlorophyllin, bacteria chlorophylls, carotenoids, lycopene, enzymes, monoclonal antibodies, any immunological agent, genetically engineered agent, benign infectious agents, whether naturally occurring or genetically engineered (e.g. the bacteria that normally reside on the skin such as acne bacteria, etc.), antibiotics, agents which attach to sebocytes in the sebaceous gland or duct cells directly, whether by topical or systemic agents that localize in these target tissues, including antibodies or antibody-chromophore compounds of these structures. In general, the topical agent chosen will have certain absorption characterstics that augment the penetration of the radiation to the tissue targeted for treatment, i.e., sebaceous oil gland, acne-scarred tissue, etc.

DETD [0084] Scarring is commonly seen as a consequence of disorders, diseases, or dysfunctions of the sebaceous apparatus. Scarring may consist of one or more of the following: raised hypertrophic scars or fibrosis, depressed atrophic scars, hyperpigmentation, hyperpigmentary redness or telangectasia. Raised or thick or hard hypertrophic scars (which are composed of an excess of collagen) can be improved by photomodulation wherein the stimulation of production of collagen dissolving enzymes (called Matrix metalloproteinases) such as **MMP-1 (collagenase)** causes the **scar** tissue to be diminished. Such photomodulation can be accomplished alone or in combination with photothermal methods (see FIGS. 14-38, wherein MMP-1 can be seen to be increased by the traditional photothermal methods--at around 7.0J/cm2 energy levels, although MMP-1 also can be stimulated in the non thermal photomodulation light energies). FIG. 13 shows enlarged tissue photographs of new collagen growth produced by the present invention.

ACCESSION NUMBER: 2003:4510 USPATFULL

TITLE: Low intensity light therapy for the manipulation of fibroblast, and fibroblast-derived mammalian cells and collagen

INVENTOR(S): McDaniel, David H., Virginia Beach, VA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003004556	A1	20030102
APPLICATION INFO.:	US 2002-119772	A1	20020411 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-819081, filed on 15 Feb 2001, PENDING Division of Ser. No. US 1998-203178, filed on 30 Nov 1998, GRANTED, Pat. No. US 6283956

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Wayne C. Jaeschke, Jr., Morrison & Foerster LLP, Suite 5500, 2000 Pennsylvania Avenue, N.W., Washington, DC, 20006-1888

NUMBER OF CLAIMS: 28

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 38 Drawing Page(s)

LINE COUNT: 2030

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L35 ANSWER 2 OF 192 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:251940 CAPLUS
DN 136:241710
TI Treatment of **acne** using lipoic acid
IN Perricone, Nicholas V.
PA USA
SO U.S., 7 pp., Cont.-in-part of U.S. Ser. No. 415,792.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-38
ICS A61K031-355; A61K031-045; A61K031-07
NCL 514448000
CC 1-12 (Pharmacology)
Section cross-reference(s): 62
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6365623	B1	20020402	US 1999-475514	19991230
	US 5965618	A	19991012	US 1997-971820	19971117
	US 6472432	B1	20021029	US 1999-415792	19991008
	WO 2001049250	A2	20010712	WO 2001-US63	20010102
	WO 2001049250	A3	20020110		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2001004872	A	20020213	BR 2001-4872	20010102
	EP 1185257	A2	20020313	EP 2001-901666	20010102
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003519165	T2	20030617	JP 2001-549619	20010102
PRAI	US 1997-971820	A2	19971117		
	US 1999-415792	A2	19991008		
	US 1999-475514	A	19991230		
	WO 2001-US63	W	20010102		

AB Active **acne** and **acneiform** scars are treated by topical application of a compn. contg. lipoic acid and/or a lipoic acid deriv. such as dihydrolipoic acid, a lipoic or dihydrolipoic acid ester, a lipoic or dihydrolipoic acid amide, a lipoic or dihydrolipoic acid salt, and mixts. of any of these to **reduce** erythema, pore size, and **scarring**. Topical application of lipoic acid and/or a lipoic acid derivs. are advantageously used with at least one adjunct ingredient such as a **retinoid**, an antibiotic, or benzoyl peroxide conventionally used for **acne**, alone or in combination with dimethylamino alc., an .alpha.-hydroxy acid such as glycolic acid, a tyrosine, tocotrienol, and/or a fatty acid ester of ascorbic acid. One preferred embodiment contains a combination of lipoic acid, an .alpha.-hydroxy acid, and dimethylamino alc. In an example given use of a lipoic acid or lipoic + glycolic acid prepns. by patients with **acne** vulgaris and/ot **acneiform scars** markedly **reduced** erythema, pustules, papules and comedones.

ST **acne** treatment lipoate glycolate dimethylaminoethanol

IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino; treatment of **acne** using lipoic acid in combination with an .alpha.-hydroxy acid and dimethylamino alc.)

L27 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

IT **Flavonoids**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bio-, Ginkgo; topical medicament contg. compds. with vasokinetic activity for **treatment of wounds and scars**)

IT **Flavonoids**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxo, Ginkgo biloba; topical medicament contg. compds. with vasokinetic activity for **treatment** of wounds and **scars**)

AN 1995:997258 CAPLUS

DN 124:66591

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 680761	A1	19951108	EP 1995-105944	19950420
	EP 680761	B1	20011219		
	R: DE, ES, FR, GB, IT, SE				
	ES 2080037	T3	20020701	ES 1995-105944	19950420
	JP 08040876	A2	19960213	JP 1995-108720	19950502
	CA 2148632	AA	19951107	CA 1995-2148632	19950504
	AU 9517886	A1	19951116	AU 1995-17886	19950504
	AU 710197	B2	19990916		
	US 5795575	A	19980818	US 1996-763925	19961212
	HK 1012568	A1	20020726	HK 1998-113939	19981217

L27 ANSWER 4 OF 9 USPATFULL on STN

DETD [0023] Our invention teaches that cellulites may be treated effectively by using biochemical agents that are derived from plants which are capable of selectively blocking the action of endogenous estrogen and stimulating lipolysis. Specifically, the use of **genistein** blocks the action of estradiol on the estrogen receptor in the fibroblast of the connective tissue. More specifically, this receptor appears to be the estrogen receptor .beta.. By blocking this receptor, the fibroblasts in the area of the cellulite will not be stimulated to produce more **collagenase** and elastase. This action allows the body to affect a repair of the damaged connective tissue. At the same time, **genistein** is capable of stimulating lipolysis in the area of cellulite..sup.6 **Genistein** is known to inhibit tyrosine kinase which promotes the formation of the matrix metalloprotein **collagenase** from fibroblasts..sup.7 .sup.6Kuppusamy, U R, and Das, N P. Effects of flavanoids on cyclic AMP phosphodiesterase and lipid mobilizations in rat adipocytes. Biochem Pharmacol 44:1307-1315, 1992. .sup.7Akiyama, T et al **Genistein** a specific inhibitor of tyrosine kinase. J. biol Chem 262:5592-5, 1987.

DETD [0026] 1. An isoflavone, such as **genistein**, diadzein, or other isoflavones, that have an affinity for estrogen receptors on fibroblasts. The competitive action blocks the stimulation of estrogen to produce **collagenase**.

ACCESSION NUMBER:	2002:198294 USPATFULL			
TITLE:	Formulation of flavones and isoflavones for treatment of cellulite			
INVENTOR(S):	Pugliese, Peter T., Berneville, PA, UNITED STATES			

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002106388	A1	20020808	
APPLICATION INFO.:	US 2001-989019	A1	20011121	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-250397P	20001124 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	ARTHUR R. EGLINGTON, 113 Cross Creek Dr. R.D. # 5., Pottsville, PA, 17901
NUMBER OF CLAIMS:	11
EXEMPLARY CLAIM:	1
LINE COUNT:	444

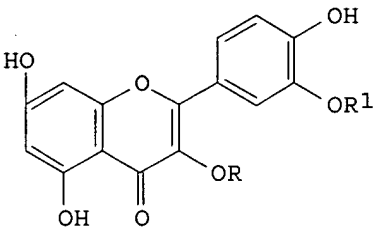
Copy #2

L6 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2002 ACS
AN 1984:451606 CAPLUS
DN 101:51606
TI Interaction in the antibacterial activity of flavonoids from Sophora japonica L. to Propionibacterium
AU Kimura, Masayuki; Yamada, Hiromi
CS Yakult Inst. Microbiol. Res., Kunitachi, 186, Japan
SO Yakugaku Zasshi (1984), 104(4), 340-6
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
CC 10-5 (Microbial Biochemistry)
Section cross-reference(s): 63
AB The antibacterial activities of several crude drugs to bacteria were examd. by the agar diffusion method using paper disks, and it was found that the EtOH ext. of flower buds of S. japonica showed antibacterial activity against P. **acnes**, P. avidum, and Staphylococcus aureus under weak acidic conditions. After purifn. of the ext., the activity was attributed to the interaction caused by 3 components: **quercetin** (I), rutin (II), and isorhamnetin-3-rutinoside (III). When I, II, and III were applied singly, only I showed very weak activity, and the others not at all. By mixing I and II, or I and III, 50% and 70% activity of the EtOH ext. appeared, resp. Moreover, after mixing the 3 flavonoids, the full activity of the ext. was recovered. A small amt. of kaempferol-3-rutinoside was also obtained from the EtOH ext. This compd. had a similar effect to III but was weaker. Examn. of the drug interaction in a liq. culture system showed that the antibacterial activity of the system increased with an increase in the soly. of I caused by II. Thus, the active principle is I, and by the addn. of II, the soly. of I increases to increase the apparent activity. A similar increase in the activity of I by the addn. of III is thought to be based on the same mechanism as that of II.
ST Sophora flavonoid bactericide Propionibacterium
IT Sophora japonica
(flavonoids from flower bud ext. of, antibacterial activity of)
IT Propionibacterium acnes
Propionibacterium avidum
Staphylococcus aureus
(flavonoids of Sophora japonica flower buds sensitivity to)
IT Microbicidal and microbiostatic action
(bactericidal, of flavonoids, soly. in relation to)
IT Glycosides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(flavonoid, antibacterial activity of, to Propionibacterium)
IT 153-18-4 604-80-8 17650-84-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antibacterial activity of quercetin and, soly. in relation to)
IT 117-39-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antibacterial activity of, soly. in relation to)

ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 1984:460134 CAPLUS
DN 101:60134
TI Skin lotions for treatment of Propionibacterium acnes
PA Yakult Honsha Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC A61K031-35; A61K007-00; A61K031-70
ICA C07D311-30; C07H017-06
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 59044313	A2	19840312	JP 1982-154598	19820907
JP 02001806	B4	19900112		

GI



I, R=R1=H
II, R=?-rhamnosyl-?-glucosyl, R1=H
III, R=?-rhamnosyl-?-glucosyl, R1=Me

AB Microbicidal formulations, esp. effective against P. **acnes** on the skin, contain **quercetin** (I) [117-39-5] in combination with rutin (II) [153-18-4] and/or isorhamnetin 3-O-rutinoside (III) [604-80-8]. Thus, I 0.6, II 2.0, and III 0.4 g were dissolved in a mixt. of 70 mL EtOH and 30 mL 0.05M .alpha.-hydroxybutyrate buffer (pH 5.0) to obtain a skin lotion.
ST quercetin isorhamnetin rutin microbicide; Propionibacterium quercetin isorhamnetin rutin; acne flavonoid
IT Propionibacterium acnes
(control of, quercetin and isorhamnetin rutinoside and rutin for)
IT Acne
(treatment of, with skin lotion contg. isorhamnetin rutinoside and quercetin and rutin)
IT 153-18-4
RL: BIOL (Biological study)
(skin lotion contg. isorhamnetin rutinoside and quercetin and, for acne treatment)
IT 117-39-5
RL: BIOL (Biological study)
(skin lotion contg. isorhamnetin rutinoside and rutin and, for acne treatment)
IT 604-80-8
RL: BIOL (Biological study)
(skin lotion contg. quercetin and rutin and, for acne treatment)

Copy # 3

L13 ANSWER 14 OF 71 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:17588 CAPLUS
DOCUMENT NUMBER: 114:17588
TITLE: Sebaceous gland-inhibiting isoflavones
INVENTOR(S): Jokura, Yoji; Ishikawa, Shinji; Nishizawa, Yoshinori; Yoshimura, Koichi; Kitahara, Takashi; Hattori, Michihiro
PATENT ASSIGNEE(S): Kao Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02193919	A2	19900731	JP 1989-13481	19890123

OTHER SOURCE(S): MARPAT 114:17588

AB Sebaceous gland-inhibiting agents contain isoflavones I (R1, R2, R3 = H, aliph. or cyclic hydrocarbyl, C1-6 alkoxy; A, B, C, D = H, OH, MeO; R2 = C .noteq. H) as active ingredients. I control excess sebum secretion, thus preventing **acne**, and have minimal side effects even after prolonged use. Aq. acetone soln. contg. 10.0 mg luteone/mL applied topically to hamsters at 50 .mu.L 2 times/day for 4 days resulted in remarkable inhibition of testosterone propionate-induced sebum secretion. A cosmetic prepn. was formulated contg. glycerin ether 1.50, polyoxyethylene hydrogenated castor oil 1.50, sorbitan monostearate 1.00, squalane 10.00, dipropylene glycol 5.00, **genistein** 0.10, and H2O to 100% by wt.

ST sebaceous gland inhibitor isoflavone; **acne** treatment isoflavone; **genistein acne** treatment

IT **Acne**
(treatment of, isoflavones for)

IT **446-72-0**, **Genistein** 548-77-6, Tectorigenin
1156-78-1, 2'-Hydroxygenistein 41743-56-0, Luteone
RL: BIOL (Biological study)
(sebaceous gland-controlling agents contg.)

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Copy #4

L13 ANSWER 13 OF 71 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:209989 CAPLUS
DOCUMENT NUMBER: 124:241803
TITLE: Skin-conditioning compositions containing isoflavone
INVENTOR(S): Brunke, Reinhold A.
PATENT ASSIGNEE(S): New Standard Gmbh, Germany
SOURCE: Ger. Offen., 4 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4432947	A1	19960321	DE 1994-4432947	19940916
DE 4432947	C2	19980409		

AB Skin care compns. contg. isoflavone and its derivs. act as radical scavengers which prevent aging of the skin, as dermal angiogenesis inhibitors, and as antiproliferative agents against melanomas, and are useful for treatment of varicose veins, **acne**, fatty skin, graying of the hair, pigment spots, and alopecia. Thus, a gel for treatment of **acne** was prepd. by combining a mixt. of Eumulgin B1 3, Cetiol 868 10, methylparaben 0.15, propylparaben 0.10, and soybean ext. (source of isoflavones) 10.0 wt.% with H2O 73, Sepigel 305 3.5, and Kathon CG 0.05 wt.%.

ST skin conditioner isoflavone; **acne** treatment isoflavone; angiogenesis skin isoflavone; baldness treatment isoflavone

IT **Acne**
Alopecia
(treatment of; skin-conditioning compns. contg. isoflavones)

IT **446-72-0**, 5,7,4'-**Trihydroxyisoflavone** 480-23-9, 3',4',5,7-Tetrahydroxyisoflavone 486-66-8, 7,4'-Dihydroxyisoflavone 491-80-5, 5,7-Dihydroxy-4'-methoxyisoflavone 529-59-9, Genistin 529-60-2 548-76-5 552-66-9, Daidzin 574-12-9, Isoflavone 574-12-9D, Isoflavone, derivs. 2284-31-3 34086-51-6
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(skin-conditioning compns. contg. isoflavones)

L35 ANSWER 10 OF 38 USPATFULL

DETD The compounds in this invention can also be given orally in combination with compounds that bind or modify the activity of the vitamin D receptor or in combination with compounds that bind or modify the activity of the **retinoid** X receptors or **retinoic** acid receptors to provide for a synergistic effect in the treatment or prevention of the disorders listed in Tables II, III, IV, V, VI & VII. Examples of such compounds that provide for synergistic effect when given in combination with the drugs encompassed by the current invention include vitamin D analogs, various **retinoic** acid derivatives, and other ligands for **retinoid** X receptors or **retinoic** acid receptors including but not limited to compounds such as LG100268, tazarotene, TTNPB, or LGD1069 (Targretin), and RXR/PPAR heterodimeric ligands, e.g. LG101754 (Ligand Pharmaceuticals) (see, U.S. Pat. No. 6,004,987 Demarchez, et. al., Dec. 21, 1999, Use of ligands which are specific for RXR receptors.).

DETD In certain aspects, the compounds in the invention can also be given systemically (oral administration preferred) or topically in combination with natural or synthetic ligands (agonist or antagonist ligands) that bind and modify the activity of the estrogen (nuclear) receptor (ER), which include the alpha and/or the beta isoforms, i.e. ER-alpha or ER-beta or both ER-alpha and ER-beta. Examples of ER-alpa and/or ER-beta ligands are: estradiol, selective (synthetic) estrogen receptor modulators such as raloxifene, anti-estrogens such as tamoxifen and hydroxytamoxifen, and the naturally occurring phytoestrogens such as the isoflavones **genistein**, diadzein and glycitein.

DETD Synergistic therapeutic effects can be achieved by oral administration of the drugs encompassed in the current invention together with orally or intravenously administered drugs that bind to and or modify the activity of either the vitamin D receptor or **retinoid** X receptors or **retinoic** acid receptors. As such, in another embodiment, the present invention relates to a method of treating a PPAR.gamma. mediated disease, comprising administering a combination therapy of a compound of Formulae I, II or III and a member selected from the group consisting of a drug that bind to or modifies the activity of a vitamin D receptor, a **retinoid** X receptor, or a **retinoic** acid receptor.

DETD A preferred dosage range for administration of a **retinoic** acid derivative or **retinoid** would typically be from 0.1 to 100 mg per square-meter of body surface area, depending on the drug's ability to bind to or modify the activity of its cognate nuclear receptor, given in single or divided doses, orally or by continuous infusion, two or three times per day. For synergistic therapy, the preferred dosages and routes and frequency of administration of the vitamin D analogs or **retinoid** compounds can be similar to the dosages and routes and frequency of administration ordinarily recommended for these agents when given without compounds of Formulae I, II or III. Examples of effective **retinoids** are 9-cis-**retinoic** acid, 13-cis-**retinoic** acid, all-trans-**retinoic** acid (at-RA). Preferred **retinoids** for this purpose would include 13-cis-**retinoic** acid, tazarotene, or Targretin. A preferred dosage range for systemic administration of a vitamin D analog would typically be from 0.1 to 100 mg per square-meter of body surface area, depending on the drug's ability to bind to and or activate its cognate vitamin D receptor, given in single or divided doses, orally or by continuous infusion, two or three times per day. Examples of effective vitamin D analogs are 1,25-dihydroxy-vitamin D (1,25-(OH)2-vit D) and calcipotriene. The dosage range and routes and frequency of administration of compounds of Formulae I, II or III required to achieve synergistic effects when given with vitamin D or **retinoid** derivatives are the same as those described elsewhere in this disclosure. The preferred mode of administration of these drugs for synergistic therapeutic purposes would be orally although alternatively

one can use topical or parenteral routes of administration. Synergistic therapeutic effects can also be achieved for conditions that are treated by topical administration of vitamin D derivatives or **retinoid** related compounds such as psoriasis, **acne**, or other disorders not involving the skin described in Tables II, III, V, V, VI & VII. The dosages and the modes and frequency of administration of the vitamin D or **retinoid** related compounds for synergistic topical therapy would be similar to those ordinarily recommended for these agents when given without compounds of Formulae I, II or III. The dosage range and the modes and frequency required for topical administration of the compounds of Formulae I, II or III given in combination with vitamin D or **retinoid** related compounds are the same as those described elsewhere in this disclosure.

DETD A patient having dermal manifestations of either psoriasis vulgaris, or **acne** vulgaris, or human papilloma virus (HPV) infection (e.g., anogenital warts) is selected for therapy using the invention. A compound of Formulae I, II or III that modifies the activity of PPAR.gamma. is prepared in a cream vehicle at a concentration of 1 to 5% (weight/volume), typically 2.5% and is applied to the affected skin three times a day. After the skin lesions have subsided, therapy is discontinued.

DETD A patient having type 2 diabetes mellitus, or chronic generalized **acne**, or chronic generalized psoriasis, with or without psoriatic arthritis, or rheumatoid arthritis, or inflammatory bowel disease (e.g., ulcerative colitis) is selected for therapy. The patient weighs 80 kilograms. For infants or children the doses suggested are lowered in a linear fashion based on body weight or surface area. The female patient of child-bearing potential is given a pregnancy test to confirm that the patient is not pregnant. Provided that the patient is not pregnant and does not plan to become pregnant during treatment, a compound of Formulae I, II or III that modifies the activity of PPAR.gamma. is orally administered in a dosage of 20 to 1,000 milligrams twice daily, more typically 100 mg twice daily. The patient is monitored for improvement in the manifestations of the index disease. Additionally, a complete blood count, including white cell count and differential, a platelet count, and liver function tests (such as levels of alkaline phosphatase, lactose dehydrogenase, and transaminases) are checked prior to treatment and periodically thereafter. The dosage is tapered when the manifestations of the disease subside, or discontinued if indicated.

DETD

TABLE II

Examples of non-malignant proliferative, inflammatory disorders treatable with compounds described in this invention

Organ System Disease/Pathology

Dermatological Psoriasis (all forms), **acne** vulgaris, **acne** rosacea, common warts, anogenital (venereal) warts, eczema; lupus associated skin lesions; acute and chronic dermatitides (inflammation of the skin) such as acute and chronic eczema such as atopic dermatitis, allergic dermatitis, contact dermatitis, cosmetic dermatitis, chemical dermatitis, diaper rash, sunburn, seborrheic dermatitis and solar dermatitis; keratoses such as seborrheic keratosis, senile keratosis, actinic keratosis, photo-induced keratosis, skin aging and wrinkle formation including photo-induced skin aging, keratosis follicularis; keloids and prophylaxis against keloid formation; leukoplakia, lichen planus, keratitis, urticaria, pruritus, hidradenitis, **acne** inversa.

Cardiovascular Congestive heart failure, endarteritis, endocarditis, atherogenesis, hypertension, vasculo-occlusive

diseases including atherosclerosis, thrombosis and restenosis after angioplasty; acute coronary syndromes such as unstable angina, myocardial infarction, ischemic and non-ischemic cardiomyopathies, post-MI cardiomyopathy and myocardial fibrosis, substance-induced cardiomyopathy.

Endocrine Insulin resistant states including obesity, diabetes mellitus (types 1 & 2), diabetic retinopathy, macular degeneration associated with diabetes, gestational diabetes, impaired glucose tolerance, polycystic ovarian syndrome; osteoporosis, osteopenia, accelerated aging of tissues and organs including Werner's syndrome and Wasting syndrome (all etiologies).

Urogenital Endometriosis, benign prostatic hypertrophy, leiomyoma, polycystic kidney disease, diabetic nephropathy.

Pulmonary Asthma, chronic obstructive pulmonary disease (COPD), reactive airway disease, pulmonary fibrosis, pulmonary hypertension.

Immunological/ Rheumatoid arthritis, Raynaud's phenomenon/disease,
Connective tissue/ Sjogren's syndrome systemic sclerosis, systemic lupus
Joints erythematosus, vasculitides, ankylosing spondylitis, osteoarthritis, reactive arthritis, psoriatic arthritis, fibromyalgia.

Other Fibrocystic breast disease, fibroadenoma, chronic fatigue syndrome.

ACCESSION NUMBER: 2002:45631 USPATFULL
TITLE: 1,2-dithiolane derivatives
INVENTOR(S): Pershadsingh, Harrihar A., Bakersfield, CA, United States
Avery, Mitchell A., Oxford, MS, United States
PATENT ASSIGNEE(S): University of Mississippi, University, MI, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6353011	B1	20020305
APPLICATION INFO.:	US 2000-520208		20000307 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-497324, filed on 3 Feb 2000, now patented, Pat. No. US 6204288
Continuation-in-part of Ser. No. US 1999-264370, filed on 8 Mar 1999, now patented, Pat. No. US 6127394
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Gerstl, Robert
LEGAL REPRESENTATIVE: Townsend and Townsend and Crew, LLP
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Figure(s); 15 Drawing Page(s)
LINE COUNT: 2266
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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DETD . . . adult, (komedonenakne, papulOese,
pustulOese, knotige d. h. nodulAere, nodulozystische Akne)
Z
Akne conglobata, (Sonderform: Hidradenitissupprativa)
Akne fulminans
Akne - Tetrade
Akne neonatorum
Altersakne (M. Favre - Racouchot)
Mechanische Akneformen(**Acne** excoriee)
Akne cosmetica
Follikulitis bei superinfizierter Akne (Stapylokokken)
berufsbedingte Akneformen (z. B. Chlorakne)
IV. Herpesvirus - Infektionen.
. . .
der Gruppe Quercitin, Rutin, Chrysin,
Kaempferol, Myricetin, Rhamnetin, Apigenin, Luteolin, Naringin,
Hesperidin, Naringenin, Hesperitin, Morin, Phloridzin, Diosmin, Fisetin,
Vitexin, Neohesperidin Dihydrochalkon, Flavon, Glucosylrutin und
Genistein.
. . .
Ascorbylpalmitate, Mg -
Ascorbylphosphate, Ascorbylacetate, Ascorbylglycoside),
Tocotrienole,Tocopherole und deren Derivate (z.B. Vitamin E - acetat,
alpha-, beta-, gamma-, delta-Tocopherole, Tocopherylglycoside), Vitamin
A und Derivate (**Retinol**, Vitamin A - palmitat, Vitamin A -
SAeure) sowie
Konyferylbenzoat des Benzoeharzes, wAessrige oder alkoholische Tabak-,
Tee- undloder Kaffee - Extrakte, Teein,. . .

CLMDE. . . der Gruppe Quercitin, Rutin, Chrysin,
Kaempferol, Myricetin, Rhamnetin, Apigenin, Luteolin, Naringin,
Hesperidin, Naringenin, Hesperitin, Morin, Phloridzin, Diosmin, Fisetin,
Viteyin, Neohesperidin Dihydrochalkon, Flavon, Glucosylrutin und
Genistein, alpha-Glucosylrutin, alpha-Glucosylmyrictr in,
alpha-
Glucosylisoquercitrinitrin und alpha-Glucosylquercitrin, alpha-
Glucosylrutin, alpha-Glucosylmyrictrin, alpha-Glucosylisoquercitrinitrin
und alpha-Glucosyiquercitrin.

ACCESSION NUMBER: 1996018381 PCTFULL ED 20020514
TITLE (ENGLISH): AGENTS ACTING AGAINST HYPERREACTIVE AND HYPOACTIVE, DEFICIENT SKIN CONDITIONS AND MANIFEST DERMATITIDES
TITLE (FRENCH): AGENTS EFFICACES CONTRE DES ETATS CUTANES DEFICIENTS HYPER-REACTIFS OU HYPO-ACTIFS ET DES DERMATITES MANIFESTES
INVENTOR(S): LANZENDoeRFER, Ghita; STAeB, Franz; UNTIEDT, Sven
PATENT ASSIGNEE(S): BEIERSDORF AG; LANZENDoeRFER, Ghita; STAeB, Franz; UNTIEDT, Sven
LANGUAGE OF PUBL.: German
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9618381	A1	19960620

DESIGNATED STATES JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1995-EP4907 A 19951212
PRIORITY INFO.: DE 1994-P 44 44 238.6 19941213

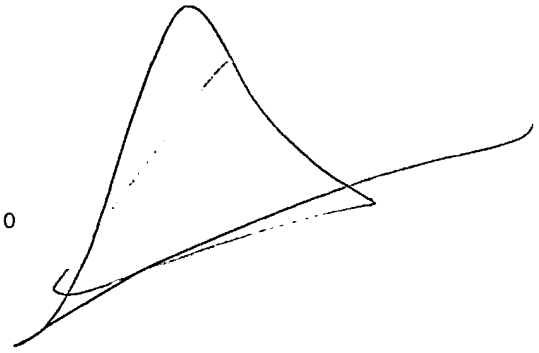
L48 ANSWER 44 OF 45 PCTFULL COPYRIGHT 2002 Univentio

DETD . . . 5,614,201 and U.S. Patent
5,482,710, both to Slavtcheff et al. These mask products

are reported to eliminate pimples, blemishes and the redness of **acne**. Unfortunately delivery via masks requires the presence of significant amounts of water which may adversely react with moisture sensitive ingredients. Extended drying times. . .

Vitamin A for purposes of this invention include **retinol**, **retinoic** acid as well as retinyl C2_C22 fatty acid esters.

. . .
Ursi (bearberry) 0
vanilla fruit w
borage seed oil 0
wild borage seed oil 0
Flavanoid Extracts
hesperedin 0
neohesperidin w
quercetin 0
rutin w
morin w
kaempherol 0
mVricet n w/o
genistein 0
Phytoestroagn ExtractB
coumestrol 0
estriol 0
phytosterols 0
Other Extracts
limonene 0
ethoxvauin 0
chlorogenic acid w
glutathione w
hydroquinone 0
ubiauinone (coenzyme Q) 0
lipoic acid 0
N-acetyl cysteine 0
curcumin 0
Herbal. . .



ACCESSION NUMBER: 1998042303 PCTFULL ED 20020514
TITLE (ENGLISH): COSMETIC PRODUCT
TITLE (FRENCH): PRODUIT COSMETIQUE
INVENTOR(S): CROTTY, Brian, Andrew; MINER, Philip, Edward; JOHNSON, Anthony, William; ZNAIDEN, Alexander, Paul; COREY, Joseph, Michael; VARGAS, Anthony; MEYERS, Alan, Joel; LANGE, Beth, Anne
PATENT ASSIGNEE(S): UNILEVER PLC; UNILEVER N.V.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9842303	A1	19981001
DESIGNATED STATES	AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG		
APPLICATION INFO.:	WO 1998-EP1423	A	19980310
PRIORITY INFO.:	US 1997-60/039,378		19970320
	US 1998-60/072,355		19980123

L48 ANSWER 37 OF 45 PCTFULL COPYRIGHT 2002 Univentio

DETD . . . include, for example, dry skin, ichthyosis, palmar and plantar hyperkeratoses, dandruff, lichen simplex chronicus, Dariers disease, keratoses, lentigines, age spots, melasmas, blemished skin, **acne**, psoriasis, eczema, pruritis, inflammatory dermatoses, striae distensae (i.e., stretch marks), warts and calluses.

. . .

4,053,630 and 4,363,815, the disclosures of which are all incorporated herein by reference. Suitable therapeutic organic acids may also include derivatives of **retinoic** acid, such as 1-hydroxyretinoic acid and 1-ketoretinoic acid, as described in U.S. Patent No. 4,194,007, the disclosure of which is also incorporated. . .

. . .

The microsphere encapsulated therapeutic organic acid can be readily used in compositions containing other cosmetic and pharmaceutical agents, e.g. anti-fungals, vitamins, sunscreens, **retinoids**, antihistamines, depigmenting agents, anti-inflammatory agents, anesthetics, surfactants, emulsifiers, stabilizers, preservatives, antiseptics, emollients, thickeners, lubricants, humectants, chelating agents, fragrances, colorants and skin penetration enhancers.

. . .

present invention may also include: from about 0.01 wt.% to about 30 wt.%, preferably from about 0.05 wt.% to about 5 wt.%, **retinoids**, such as **retinol**, **retinoic** acid, retinyl palmitatejetinyl propionate or retinyl acetate as well as synthetic **retinoid** mimics; from about 0. 00 1 wt. % to about 1 0 wt. % hormones such as estriol or estrad iol;. . .

quercetin, rutin, daidzein, **genistein**), ferrulic acid derivatives (e.g. ethyl ferrulate, sodium ferrulate), and 6-hydroxy-2,5,7,-tetramethyl-chroman carboxylic acid. The compositions may also contain effective concentrations of water-soluble antioxidants,. . .

CLMEN. . . 3, wherein said composition further comprises at least one additional agent selected from the group consisting of antifungals, vitamins, sunscreens, keratolytic agents, **retinoids**, antiallergenic agents, depigmenting agents, antiinflarnmatory agents, anaesthetics, surfactants, moisterizers, exfolients, emulsifiers, antioxidants, insect repellents sunscreen agents, stabilizers, preservatives, antiseptics, emollients, thickeners, lubricants, humectants, chelating. . .

ACCESSION NUMBER: 1999055307 PCTFULL ED 20020515

TITLE (ENGLISH): METHOD OF TREATING THE SKIN WITH ORGANIC ACIDS IN ANHYDROUS POLYMERIC DELIVERY SYSTEMS

TITLE (FRENCH): PROCEDE DE TRAITEMENT DE LA PEAU PAR DES ACIDES ORGANIQUES DANS DES SYSTEMES D'ADMINISTRATION POLYMERES ANHYDRES

INVENTOR(S): CURTIS, Ernest, S.; KALAFSKY, Robert; KAPLAN, Elinor, R.

PATENT ASSIGNEE(S): AVON PRODUCTS, INC.

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

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	WO 9955307	A1	19991104

DESIGNATED STATES: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 1999-US7473 A 19990405
PRIORITY INFO.: US 1998-09/069,089 19980428

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ABEN . . . on human skin (i.e., chronological aging of human skin) can be prevented and treated with the topical application of a **retinoid**, preferably **retinol**. We have found that some of the same pathways (namely the stress-activated pathways, SAPs) activated in photoaging of human skin. . . that other pathways (namely the mitogen-activated ERK pathway) is depressed in the same skin. Treatment of chronologically-aged skin with a **retinoid** both inhibits degradation of dermal collagen and promotes procollagen synthesis. Biopsied sections from skin of elderly (80+ years old) show. . .

ABFR . . . du temps sur la peau humaine (c. -a-d. le vieillissement de la peau humaine du a l'age) par l'application topique d'un **retinoide**, de preference du **retinol**. Il a ete decouvert que certaines voies (a savoir les voies activees par le stress, SAP) activees au cours du. . . voie ERK activee par mitogenes) sont faibles dans ladite peau. Le traitement de peau de personnes agees a l'aide d'un **retinoide** permet d'inhiber la degradation de collagene dermique et de favoriser la synthese de procollagene. Des coupes de biopsies de peau. . .

DETD This invention relates to methods and compositions, especially those comprising **retinoids**, preferably topically applied, which are useful for improving keratinocyte and fibroblast proliferation, decreasing matrix metalloproteinase (MMP) expression, and improving collagen synthesis in. . .

. . .

EP-A2-0 379,367 describe a method for the treatment or prevention of intrinsically aged skin with retinolds. Kligman et al. tested all trans- **retinoic** acid (as Retin-A' cream) on albino hairless mice and on 5 elderly caucasian respectively; see also U.S_ Pat. No. 3,060,229. Retinal. . . wrinkles, warts, psoriasis, eczema, dandruff, and the like (see EP-A2-0 391 033). There is also 'dence to indicate that tretinoin (all trans **retinoic** acid) improves the appearance of evi I I 1 photoaged skin. Albert M. KlIgman, Current Status of Topical Tretinoin in the

Treatment of. . .
. . .
naringenin and/or quereetin, and a retinold. The compositions are described as useful for treating many unrelated skin conditions, such as wrinkles, **acne**,
skin lightening, and age spots. The action of their composition on human skin is
described with respect to an enzyme (transglutaminase) important. . .
. . .
promote procollagen synthesis, the
application preferably being performed on a regular basis. A preferred class of
compounds that perform both functions are **retinoids**,
especially **retinol** and all
trans-**retinoic** acid.
. . .
procollagen levels can be increased in aged human
skin by the preferably regular application to the skin of effective amounts of a
retinoid; in preferred embodiments, the treatment also
includes inhibition of collagen
degradation by the use of an MMP inhibitor.
. . .
and fibroblasts, each beneficial to the integrity of the skin, are each increased in number by the topical application of a **retinoid**,
again applied preferably
on a regular basis. Fibroblasts are trophic to the epidermis; under normal conditions
they secrete a number of growth. . .
. . .
in the skin, and increasing ERK activity, both in aged skin, by
the topical application of an effective amount of a **retinoid**
to the aged skin.
. . .
epidermal thickness (II Q, and keratinocyte density (II D) in elderly (80+ years old) skin upon application of a retinold (1% **retinol**
; one application,
occluded, and examined seven days later).

5
Fig. 12 depicts the effect of **retinoid** (**retinol**)
treatment on the growth of human
keratinocytes and fibroblasts cells cultured ex vivo from biopsy samples.
. . .
13B), an elderly individual (13C and 13D), and the same elderly individual (13E and 13F) after a single application of 1%
retinol (occluded, left for
seven days, then blopsied).
. . .
effect on activities of three MMP enzymes (MMPs 1, 2, and 9; analogous to Fig. 4) after a single application of **retinol** to
elderly skin as determined
by biopsy.

Fig. 15 depicts the **retinoic** acid-mediated induction of Type I collagen synthesis
in cultured human skin fibroblasts.

Fig. 16 depicts the in vivo induction of Type III procollagen al(III) mRNA
caused by **retinol** administration to elderly skin.

Fig. 17 depicts the in vivo induction ERK activity caused by

retinol
administration to elderly skin.

. . .
18 is a photomicrograph showing in stained sectioned biopsies of elderly skin
that, seven days after a single application of 1% **retinol**,
c-Jun protein is decreased and
the amounts of Types I and III procollagen in the skin are increased.

. . .
Our invention is generally directed to the topical administration, preferably on a
regular basis, of an amount of a retinold, preferably **retinol**
or **retinoic** acid, to the skin
of an elderly person in amounts effective to induce the proliferation of at least one of
keratinocytes and. . .

. . .
of chronologically-aged skin, 17 subjects having an
age of at least 80 years old were given one topical treatment with 1% **retinol** or with
vehicle alone, the test area was occluded for seven days, and the test area was then
blopsied. The vehicle was. . . reference to Fig. 2, namely the
number of fibroblasts and keratinocytes, the epidermal thickness, and undesirable
dermal connective tissue features. In comparing **retinol**
-treated skin with vehicle-
treated skin from the same individuals, as shown in Fig. 11, there were increased
numbers of keratinocytes (I IA) and fibroblasts (I ID) per section in the **retinol**-treated
skin (273% ($p < 0.001$) and 30% ($p < 0.05$) mean increases, respectively). In addition,
I id treatment increased the epidermal thickness substantially (II Q. Due to the
ret nol I I
short duration of the retinold (**retinol**) treatment, little
change in the number of
detrimental dermal connective tissue features (II B) was apparent.

Figs. 12A and 12B demonstrate the effects of 7-day in vivo
retinol treatment on
ex vivo growth of keratinocytes and fibroblasts extracted from biopsies of
sun-protected skin take from our individual volunteers over age 80. That is, an elderly
1 5 volunteer was treated with **retinol** (one application of 1%
retinol, occluded for seven
days), the treated area was biopsied, and the keratinocytes and fibroblasts from the
biopsy were cultured ex vivo. This **retinol** treatment of the
cells in vivo resulted in a
substantial increase in the ex vivo growth of both cell types. In. . .
30% (12A) while fibroblast growth increased
by about 200% (12B), with $p < 0.05$ for both. Accordingly, the topical application of
a **retinoid** to aged skin would be expected to increase the
number of keratinocytes
and/or the number of fibroblasts in the skin.

Figs. 13E and 13F depict **retinol**-treated, sun-protected skin
from the same
individual from whom the biopsy shown in Figs. 13C and 13D was taken,
after 7 days

having been treated as described previously (one application of **retinol**). The changes
to the skin shown are quite remarkable and unexpected. The epidermis thickened, the
interfacial surface area increased as evidence by. . .
. . .
14C depict the
average MMP activity levels (for collageriase MMP-I and gelatinases MMP-9 and
MMP-2, respectively) after treatment of elderly individuals with **retinol**. As shown in
Fig. 14, seven days after a single **retinol** treatment, the activities of MMP-I and
1 2
MMP-9 were both decreased (48% and 39% decreases, respectively, with $p < 0.001$
for both. . . from seven
volunteers over 80 years old and cultured fibroblasts from biopsy samples of their
unexposed (sun-protected) skin, we found that a **retinoic** acid concentration of
0.25 gg/ml increased the relative expression of collagen three fold from that of
untreated cells, and 0.5 and 1.0. . .

Seven 80+ year old individuals were treated clinically with 1% **retinol** cream,
applied once to sun-protected skin, covered with a patch, and left undisturbed for
seven days. Biopsies of these treated areas under. . .

Using the same technique as previously described for **retinoid** treatment
(1% **retinol** applied to sun-protected skin, occluded, and examined seven days later),
we treated and then tested three of our 80+ year old volunteers to determine the effect
of **retinoid** treatment on ERK activity. The results of biopsies from these individuals
show that after the treatment ERK activity in vivo was. . .
. . .
MMP formation and is formed by the heterodimerization of c-Jun and c-Fos proteins. Fig. 18A shows that after one week of **retinoid** (
retinol, ROL) treatment,
the c-Jun level in elderly skin (c-Jun being stained red) is significantly reduced (almost
13
absent) when compared with a biopsied. . . dermis in Fig. 18C is an artifact of the section made;
there is clearly a higher level of staining in the **retinol** treated section than in the
vehicle treated section.)
Accordingly, in one embodiment the invention comprises a method of rejuvenating aged skin by the. . .
. . .
Preferred treatment and maintenance regimes use an effective amount of about 0.4%
id, although higher doses can be used where warranted. **Retinol** is the preferred
retinol I I
'd.

retinol
In another embodiment, the invention provides a method of inducing in

vivo
keratinocyte and/or fibroblast proliferation by the topical
administration of an effective,
non-toxic amount of a retinold (preferably **retinol** or all
trans **retinoic** acid) for an
effective period of time. Again, treatment is preferably daily, once or
twice, with the
amount of retinold preferably being. . .

. . .
the topical administration of an effective amount
of a retinold for an effective period of time; again the preferred
retinolds are **retinoid**
and all trans **retinoic** acid. Again, treatment is preferably
daily, once or twice, with the
amount of retinold preferably being about 0.1%,to about 1.0%.

. . .
reduced cell growth that results, ultimately, in aged skin. Our results
shown in
Figs. 15-17 prove the in vivo effectiveness of **retinoid**
treatment in increasing the
activity level of ERK and the production Types' I and III procollagen .

. . .
the face and hands. Taken with the teachings of the
aforementioned patent and provisional applications directed to
photoaging, daily
application of a **retinoid** to the skin will ameliorate the
effects of natural aging as well
as the sun's exacerbating effects on natural aging of. . .

. . .
decreased amounts of c-Jun,
and increased amounts of Types I and/or III procollagen. Using the same
technique
described for retinold treatment (1% **retinol** applied to
sun-protected skin, occluded,
and examined seven days later), we tested three of our 80+ year old
volunteers. The
results of. . .

. . .
which
MMPs are produced naturally. Aspirin and E5510 (described by Fujimorl,
T., et at.,
Jpn J Pharmacol (1991) 55(l):81-91) inhibit NF-KB activation.
Retinoids such as those
disclosed in U.S. Pat. No. 4,877,805 and the dissociating retinolds that
are specific for
AP-1 antagonism (such as those. . . Enhancing the Therapeutic Use of
1,25(OH)2D3), filed April 4, 1997, the
disclosure of which is incorporated herein by reference. Other
retinolds, besides
retinol, include natural and synthetic analogs of vitamin A (
retinol), vitamin A
aldehyde (retinal), vitamin A acid (**retinoic** acid (RA)),
including all-trans, 9-cis, and
1 6
-cis **retinoic** acid), etretinate, and others as described in
EP-A2-0 379367,
US 4,887,805, and US 4,888,342 (the disclosures of which are all
incorporated herein
by reference). Various synthetic **retinoids** and compounds
having **retinoid** activity are
expected to be useful in this invention, to the extent that they exhibit
retinoid activity
in vivo, and such are described in various patents assigned on their
face to Allergan

Inc., such as in the following. . . 5,677,451; 5,677,323; 5,677,320; 5,675,033; 5,675,024;
5,672,710; 5,688,175; 5,663,367; 5,663,357; 5,663,347; 5,648,514; 5,648,503;
5,618,943; 5,618,931; 5,618,836; 5,605,915; 5,602,130. Still other compounds
described as having **retinoid** activity are described in other
U.S. Patents, numbered.

. . .

558648 (disclosed
therein as useful for inhibiting MMI's in the treatment of, among other etiologies, skin
ulcers, skin cancer, and epidermolysis bullosa). **Retinoids** have been reported by
Goldsmith, L.A. (Physiology, Biochemistry, and Molecular Biology of the Skin, 2nd.

. . .

of possible
allergic or sensitization reactions, the topical administration of tetracyclines should be
monitored carefully for such untoward reactions. Other MMP inhibitors include
genistein and quercetin (as described in US 5637703, US 5665367, and
FR-A-2,671,724, the disclosures of which are incorporated herein by reference) and
related. . .

. . .

to provide preferably about 5 @Lg/CM2 skin when applied. For example, a
preferred composition for use in this invention is Retin-A' **retinoic** acid gel and cream
(available from Ortho Pharmaceuticals for the treatment of **acne** vulgaris), in strengths
of from 0.01% to 0.1%; the vehicle preferably includes, depending upon the particular
formulation, at least one of butylated. . .

. . .

in young individuals (such as those aged 40 and younger). In
particular, we have found that a single application of 1% **retinol** to chronologically-
aged skin, covered with an air-permeable adhesive bandage, and examined seven days
later, resulted in procollagen protein levels comparable to. . . in sun-protected
skin of significantly younger individuals (e.g., under age 40). It would be more
18
preferable for elderly persons to apply the **retinoid** once or
twice daily to maintain -a
therapeutic regimen, although the agent could be applied on a less frequent but
preferably regular. . .

. . .

and so treatment of elderly skin with both a
'd and an MMP inhibitor is important for achieving the desired benefits of
retinol I I I I 1
improved procollagen blosynthesis. In fact, we have found in skin not having a
reduced level of collagen,. . .

Although **retinol** is the preferred compound for topical administration, effective
derivatives of **retinol** that would be expected to be useful for

practicing this invention
include retinal, **retinoic** acid (including all trans, 9-cis,
and 13-cis isomers) and
derivatives thereof (such as 7,8-didehydroretinoic acid), and others as
described by
Kligman et. . .
. . .
skin samples by guanidinium hydrochloride lysis and ultracentrifugation
(as described by G.J. Fisher et al., Cellular, immunologic and
biochemical
characterization of topical **retinoic** acid-treated human skin,
J Investig. DematoL,
96:699-707 (1991)). Northern analysis of total RNA (40 @ig/lane) with
randomly
12p
primed labelled cDNA probes for the particular mRNA to be determined
were
performed as described by G.J. Fisher et aL (in All ttvns
retinoic acid induces cellular
retinol-binding protein in human skin in vivo, J Investig.
DermatoL, 105:80-86
(1995)). Type III procollagen rnRNA was determined usincy reverse
transcriptase
polymerase chain. . .
. . .
nuclear extracts from human skin by Western analysis
as described by G.J. Fisher et al. (in Immunological identification and
functional
quantitation of **retinoic** acid and **retinoid** X
receptor proteins in human skin, J Biol.

CLMEN 3 The method of claim 2, wherein the rennold is selected from
retinol,
retinal,´ **retinoic** acid, a **retinoic** acid salt, a
derivative or analog thereof, or a mixture
thereof

4 The method of claim 3, wherein the retinold is **retinol** 'd.
I or **retinoic** aci

9 A method of preventing chronologically-aged skin, comprising providing
a
topically administerable, non-toxic amount of a **retinoid** in a
cosmetically suitable
vehicle and applying said **retinoid** to the skin at least once
weekly in an amount
effective to no rmalize procollagen synthesis and inhibit colla en
degradation.
9
I. . . claim 9, wherein the skin is sun-protected skin.
I 11. The method of claim 9, wherein the retinold is selected from
retinol,
retinal, **retinoic** acid, a **retinoic** acid salt, a
derivative or analog thereof, or a mixture
thereof

12 The method of claim I 1, wherein the retinold is **retinol**.

13 The method of claim 9, wherein the **retinoid** is applied
daily.
. . .
normalizing the production of procollagen in chronologically--
aged skin, comprising the steps of providing a topically administerable,
non-toxic

retinold and administering said **retinoid** to the skin in an amount effective to normalize
the production of procollagen.

15 The method of claim 14, wherein the retinold is **retinol**.

17 The method of claim 16, wherein the **retinoid** is applied daily.
24
. The method of claim 14, further comprising the step of simultaneously inhibiting the degradation of collagen, said method. . .
. . .
the activity level of ERK in aged human skin which comprises the topical application of an effective, non-toxic amount of a **retinoid**
to said skin.

23 The method of claim 22, wherein the retinold is retinold or **retinoic** acid.

25 The method of claim 22, wherein the **retinoid** is **retinol** d or **retinoic** acid.
25

ACCESSION NUMBER:	1998036742 PCTFULL ED 20020514
TITLE (ENGLISH):	METHODS AND COMPOSITIONS FOR PREVENTING AND TREATING CHRONOLOGICAL AGING IN HUMAN SKIN
TITLE (FRENCH):	PROCEDES ET COMPOSITIONS SERVANT A PREVENIR ET A TRAITER UN VIELLISSEMENT DE LA PEAU HUMAINE DU A L'AGE
INVENTOR(S):	VARANI, James; FISHER, Gary, J.; VOORHEES, John, J.; KANG, Sewon
PATENT ASSIGNEE(S):	THE REGENTS OF THE UNIVERSITY OF MICHIGAN
LANGUAGE OF PUBL.:	English
DOCUMENT TYPE:	Patent
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NUMBER	KIND	DATE
WO 9836742	A1	19980827

DESIGNATED STATES	AU BB BG BR CA CN CU CZ EE HU ID IL IS JP KR LC LT LV MK MN MW MX NO NZ PL RO SG SK SL TR TT UA UG VN GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1998-US3743	A	19980223
PRIORITY INFO.:	US 1997-60/040,594		19970225
	US 1997-60/042,976		19970407

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ABEN . . . synthesis of procollagen. This UV-induced inhibition of the synthesis of collagen can be prevented by the topical application of a **retinoid** or c-JUN
inhibitor to the skin prior to its exposure to UV radiation.
ABFR . . . synthese de procollagene. On peut empecher cette inhibition induite par UV de la synthese du collagene par l'application topique d'un
retinoide ou d'un inhibiteur de c-JUN sur la peau avant son exposition a un rayonnement UV.

DETD **Retinoids** have been used to retard the effects of photoaging in skin
appearing to have been damaged by exposure to the sun.. . .
. . .
of photoaged skin after photoaging has become apparent clinically. This patent indicates there is little point in

beginning the application of a **retinoid** to treat photodarnaged skin until the
effects of photoaging begin to appear.

. . .

then secreted from the cell upon demand, collagen is secreted continuously. According to Goldsmith, op. cit. (at 492), not only do **retinoic**
id, glueocorticolds, and vitamin D3
ac derivatives all decrease collagen synthesis,
but so do other **retinoids**.

In light of these findings, our invention generally can be summarized as
the topical administration of a **retinoid** in an amount effective to reduce the
inhibition of collagen synthesis mediated by exposure to UV radiation by applying the **retinoid** to the skin at least about 16 hours prior to exposure.

Figs. lOA-IOD depict cross-sections of biopsies of human skin treated with either **retinoic** acid or a vehicle alone and stained for the expression of
Type I procollagen mRNA, both before and after exposure of. . .

. . .

I procollagen protein in human skin after treatment with
'd or a vehicle alone, both before and after exposure of the treated
retinoic acl
skin to UV radiation, and which shows the protective effect of **retinoids** on
procollagen protein synthesis.

. . .

precursor protein in human
skin both before and after exposure to UV radiation where the exposed skin had
been treated previously with **retinoic** acid or a vehicle alone.

Figs. 13A-13D depict cross-sections of biopsies of human skin treated with either **retinoic** acid or a vehicle alone and stained for the expression of
Type III procollagen mRNA, both before and after exposure of. . .

Figs. 14A-14D depict cross-sections of biopsies of human skin treated with either **retinoic** acid or a vehicle alone and stained for the expression of
Type III procollagen protein, both before and after exposure of. . .

. . .

for
Type III procollagen protein and the pN precursor protein in human skin in vivo
where the skin was pretreated with either **retinoic** acid or a vehicle alone and
then exposed to UV radiation.

. . .

depicting our results of the assayed amount of
soluble collagen (measured via hydroxyproline content) in human skin in vivo
treated with either **retinoic** acid or a vehicle alone, both before and after
exposure to UV radiation.

Retinold Pretreatment
We tested whether retinolds, in particular all-trans **retinoic** acid, would
have any effect on the loss of procollagen mRNA and/or the procollagen

proteins in human skin after exposure to UV radiation. (Unless otherwise noted,
the **retinoic** acid used in the experiments described herein was all-trans.)
Separate areas of skin from each of our volunteers were treated with. . .
. . .
The site of the volunteers' skin to be
exposed to UV radiation was treated prior to UV exposure with either the
all-truns **retinoic** acid or the control vehicle. Pretreatment times of eight hours
before exposure did not appear to significantly prevent reduction in collagen
synthesis,. . . we describe below (in which a reduction in collagen biosynthesis was
prevented). Nevertheless, it should be understood-that a period of pretreatment
with **retinoid** more than eight and less than twenty-four hours before UV
exposure may likely be sufficient to prevent the reduction in collagen
blosynthesis we have observed. Furthermore, it should be understood that in all
of the following examples treatment with a **retinoid** (e.g., **retinoic** acid-treated)
or the vehicle (e.g., vehicle-treated) should each be understood as pretreatment
24 hours before UV exposure.

Our invention on the use of **retinoids** to protect against the UV-Induced
loss of procollagen Types I and III is more graphically depicted in Fig. 10,
which shows stained biopsy cross-sections (analogous to those shown in Fig. 1)
of vehicle- and **retinoid**-treated skin prior to UV exposure, and then after UV
exposure. Figure 10 shows cross-sections stained for Type I procollagen mRNA
(the dermis-epidermis Junction has been delineated electronically with a solid
line). Fig. 10A is vehicle-treated skin and Fig. IOB is all-trans **retinoic** acid-
treated skin, both prior to UV exposure. In this pair of photographs, the
procollagen mRNA is expressed in the various fibroblasts in the dermis; while
the **retinoic** acid-treated (RA caption in the figure) skin shows darker staining,
the number and density of the fibroblasts producing the mRNA for. . .
. . .
signalling
necessary for procollagen blosynthesis, as shown in Fig. 10D. Comparing
Figs. IOC and 10D, it is striking to note that the **retinoid**-treated skin appears
unaffected by exposure to UV radiation, to the extent that Type I procollagen
mRNA is expressed to the same degree. . .
. . .
and II B. Biopsies taken 24 hours after
exposure to UV radiation of 2MED yield striking differences between the
control and the **retinoid** treated areas. Fig. I IC shows the control (vehicle-
treated) skin biopsy in which the staining at the dermis-epidermis junction is

significantly. . .

. . .

is a histograph depicting our results of Western blot analyses of biopsies from our volunteers where the skin was pretreated with **retinoic** acid or the vehicle alone, blopsied, exposed to UV radiation, and blopsled again. As shown, prior to UV exposure the vehicle-treated area. . . has an amount of Type I procollagen and the pN collagen precursor that have been normalized to a value of 1 Unexposed **retinoic** acid-treated skin had essentially the same amounts of Type I procollagen and the pN precursor protein. The biopsies of UV-exposed skin. . . I procollagen protein and pN collagen precursor protein than were present before exposure. These results are consistent with those discussed previously. The **retinoic** acid-treated areas, though, showed very little loss of both the Type I procollagen and the pN collagen precursor protein; both values were. . .

The use of **retinoids** to protect against the UV-Induced loss of Type III procollagen is also graphically depicted in Fig. 13, which shows blopsied cross-sections. . . Type III procollagen mRNA is expressed in fibroblasts in the dermis, prior to UV exposure, in both vehicle-treated (Fig. 13A) and **retinoic** acid-treated (Fig. 13B) skin. After exposure to UV radiation, the vehicle-treated skin showed essentially a complete absence of the expression of the Type III procollagen mRNA (Fig. 13C), whereas the **retinoid**-treated skin showed little, if any, reduction in the expression of Type III procollagen mRNA (Fig. 13D).

. . .

of the Type III procollagen protein and the pN collagen precursor protein (analogous to Fig. 12) in human skin treated with either **retinoic** acid or vehicle alone prior to exposure, and blopsied both before and after UV exposure. Again, prior to UV exposure both vehicle (VEH) and **retinoic** acid (RA) treated skin had essentially the same amounts of these proteins. After 2 MEDs of UV exposure, the amounts of these proteins in the skin had been essentially halved, as shown by the VEH+UV bars. However, the **retinoic** acid-treated UV-Irradiated sections (RA+UV) had essentially the same amounts of these proteins as both the control and the **retinoic** acid-treated areas prior to exposure.

. . .

of the volunteers' skin to be treated with a id prior to UV exposure was pretreated 24 hours prior to exposure. We **retinol** pretreated certain volunteer's sun-protected skin with 0.1% all tram **retinoic** acid 8 hours prior to exposure to 2 MEDs of UV radiation. As shown in Fig. 17, the

level of soluble collagen. . . UV
exposure where the exposed skin had been pretreated with a retinold 8
hours
before exposure was essentially the same in the **retinoid**
-treated and the control
(vehicle-treated) skin. Thus, as mentioned above, to prevent UV-Induced
loss of
collagen synthesis using a retinold, pretreatment 24 hours. . .
. . .
inhibition of
collagen synthesis. These data indcate that c-JUN mediates inhibition of
type I
procollagen gene expresion by UV radiation. Accordingly, agents, like
retinoids, that block induction of c-JUN by UV radiation would
be effective in
protecting skin exposed to UV from loss of procollagen.. . .

Retinoids useful in practicing the present invention include
those such as
disclosed in U.S. Pat. No. 4,877,805 and the dissociating retinolds that
are
described by Fanjul et al. in Nature (1994) 372:104-1 10. Retihoids
typically
include natural and synthetic analogs of vitamin A (**retinol**),
vitamin A aldehyde
(retinal), vitamin A acid (**retinoic** acid (RA)), including
all-trans, 9-cis, and
13-cis **retinoic** acid), etretinate, and others as described in
EP-A2-0 379367,
US 4,887,805, and US 4,888,342 (the disclosures of which are all
incorporated
herein by reference). Various synthetic **retinoids** and
compounds having **retinoid**
activity are expected to be useful in this invention, to the extent that
they exhibit
id activity in vivo, and such are described in var' assigned on
retinol I I I ious patents I
their face to Allergan Inc., such as in the following U.S. Patents,
numbered.
. . .
the like. The
disclosures of all of the foregoing and following patents and literature
references
are hereby incorporated herein by reference. While **retinol** is
the preferred
compound for topical administration, effective derivatives of
retinol that would
be expected to be useful for practicing this invention specifically
include retinal,
id (including all-trans, 9-cis, and 13-cis isomers) and derivatives
retinoic aci I I I 1
thereof (such as 7,8-didehydroretinoic acid), and others as described by
Kligman el al., the disclosure of which. . . @.ig ± 2.5 gg/CM2
skin when applied. For example, a
provi I I
preferred composition for use in this invention is Retin-A'
retinoic acid gel and
cream (available from Ortho Pharmaceuticals) available presently for the
treatment of **acne** vulgaris, in strengths of from 0.01% to
0.1%; the vehicle
preferably includes, depending upon the particular formulation, at least
one of
butylated. . .
. . .

receptors (such as suramin, also known as an antiprotozoal),7
and antagonists of epidermal growth factor receptors (such as: AG ,
Erbstatin analog; **Genistein**; Lavendustin A; Tyrphostins 1, 9,
23, 25, 46, 47, and
51- and I'D 153035).

. . .

(e.g., ascorbyl glucoseamine), glutathione, and NAC;
and (111) other compounds such as one of the pigments that makes
tomatoes red,
lipoic acid, **genistein**, and ebselen and other selenium
compounds. Glutathione
and its precursors, such as N-acetyl cysteine (NAQ, more broadly
N-CH3(CH2),,Co cysteine (wherein n is. . .

. . .

skin samples by guanidinium hydrochloride lysis and
ultracentrifugation (as described by G.J. Fisher et al., Cellular,
immunologic
and biochemical characterization of topical **retinoic**
acid-treated human skin, J
Investig. DetmatoL, 96:699-707 (1991)). Northern analysis of total RNA
(40 gg/lane) with randomly primed 12p labelled cDNA probes for the
particular
mRNA to be determined were performed as described by G.J. Fisher el al.
(in
All trans **retinoic** acid induces cellular **retinol**
-binding protein in human skin in
vivo, J Investig. DermatoL, 105:80-86 (1995)). Type III procollagen mRNA
was determined using reverse transcriptase polymerase chain. . .

. . .

were detected in skin extracts
by Western analysis as described by G.J. Fisher et al. (in Immunological
identification and functional quantitation of **retinoic** acid
and **retinoid** X receptor
proteins in human skin, J Biol. Chem., 269- 20635 (1994)).

CLMEN 2 The method of claim 1, wherein the retinold is all-trans
retinoic
acid, **retinol**, or a mixture thereof.

27 The method of claim 26, wherein the antagonist is surarnin,
AG-494, Erbstatin analog, **Genistein**, Lavendustin A,
Tyrphostins 1, 9, 23, 25,

. . .

reduction
in collagen blosynthesis in human skin mediated by exposure of the skin
to UV
radiation, comprising an effective amount of a **retinoid** and a
pharmaceutically
acceptable carrier therefor, provided that said composition is applied
to the skin
prior to its exposure to UV radiation.

29 The composition of claim 28, wherein the retinold is all-trans
id, **retinol**, or a mixture thereof.
retinoic aci I

40 The method of claim 39, wherein the antagonist is suramin,
AG-494, Erbstatin analog, **Genistein**, Lavendustin A,
Tyrphostins 1, 9, 23, 25,

ACCESSION NUMBER: 1999051220 PCTFULL ED 20020515
TITLE (ENGLISH): METHODS AND COMPOSITIONS FOR REDUCING UV-INDUCED INHIBITION OF COLLAGEN SYNTHESIS IN HUMAN SKIN
TITLE (FRENCH): PROCEDES ET COMPOSITIONS DE REDUCTION DE L'INHIBITION DE LA SYNTHESE DE COLLAGENE INDUITE PAR UN RAYONNEMENT

UV DANS LA PEAU HUMAINE
INVENTOR(S): FISHER, Gary, J.; VOORHEES, John, J.
PATENT ASSIGNEE(S): THE REGENTS OF THE UNIVERSITY OF MICHIGAN
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9951220	A1	19991014
DESIGNATED STATES	AL AU BA BB BG BR CA CN CU CZ EE GD HR HU ID IL IN IS JP KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA UZ VN YU ZA GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG		
APPLICATION INFO.:	WO 1999-US7267	A	19990402
PRIORITY INFO.:	US 1998-60/080,437		19980402

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DETD . . . to changes
in gene expression is poorly understood. Full activation of PPARgamma and/or
PPARalpha and/or PPARdelta requires its functional dimerization with the **retinoid** X
receptor (RXR) to form PPARgamma/RXR or PPARalpha/RXR or PPARdelta/RXR. The
endogenous ligand for RXR is 9-cis-**retinoic** acid. Nutrient **retinoids** and **retinoic** acid
such as 13-all-trans-**retinoic** acid are converted to 9-cis-, 1
1 -cis-, or 13-cis-**retinoic** acid
by ubiquitous intracellular isomerases (Warrell Jr et aL, New Engl. J. Med. 329(3):177-
189 (1993)).- The full spectrum of genes that. . .
. . .
PPARgamrna, or PPARalpha, or PPARdelta, or co-activators of aijy of these
subtypes are: inflammatory skin diseases (e.g. psoriasis, atopic, dermatitis, eczema, **acne**
vulgaris, and other den-natitides), neurodegenerative diseases (e.g. multiple sclerosis,
Alzheimer's disease, Parkinson's disease), cardiovascular diseases (e.g. atherosclerosis,
venous and arterial occlusive diseases, restenosis. . .
. . .
either as a
single agent, or in combination with a natural or synthetic compounds. Such compounds
include agonists for PPARalpha, PPARdelta, PPARgamma, **retinoid** X receptor (RXR),
vitamin D receptor (VDR), glucocorticoid receptor (GR), Liver X receptor (LXR) or
LXR/RXR (e.g. an oxysterol (22(R)-hydroxycholesterol, 25-hydroxycholesterol, 7a-
hydroxycholesterol,. . .

[00571 Other nuclear receptors to which the present invention applies are: the
constitutive androstane (xenobiotic) receptor (CAR), the **retinoid** X receptor (RXR), the
pregnane X receptor, the Farnesiod X receptor, the liver X receptor, and the steroid X
receptot These nuclear. . .

[01881 The compounds can be used to treat inflammatory, proliferative or degenerative skin disease, such as psoriasis, keratitis, hidradenitis, ichthyosis, **acne** vulgaris, rosacea, verrucae and other HPV infections, atopic dermatitis, allergic dermatitis, chemical (irritant) dermatitis, seborrheic dermatitis, solar dermatitis, acute and chronic eczema, seborrheic. . .

. . .

second agent selected from the above-identified categories of compounds, administered orally, topically or intravenously. A preferred dosage range for administration of a **retinoic** acid derivative or **retinoid** would typically be from 0. I to 1 00 mg per square-meter of body surface area, depending on the drug's ability. . . times per day. For synergistic therapy, the preferred dosages and routes and frequency of administration of the vitamin D analogs or **retinoid** compounds can be similar to the dosages and routes and frequency of administration ordinarily recommended for these agents when given without PPARgarnma activators. Examples of 130 effective **retinoids** are 9-cis-**retinoic** acid, 13-cis-**retinoic** acid, all-trans-**retinoic** acid (at-RA). Preferred **retinoids** for this purpose would include 13-cis-**retinoic** acid, tazarotene, or Targretin. A preferred dosage range for systemic administration of a vitamin D analog D or **retinoid** derivatives are the same as those described elsewhere in this disclosure.

. . .

the tocopherols (e.g. vitamin E, vitamin E succinate), carotenes and carotenoids (e.g. beta-carotene), alpha-lipoic acid, probucols, flavones, isoflavones and flavonols (e.g. quercetin, **genistein**, catechin, apigenin, lutein, luteolin), glutathione and its derivatives (e.g. N-acetylcysteine and dithiothreitol), and phytoestrogens and phenolic anthocyanidin and procyanidin derivatives (e.g. resveratrol, cyanidin,. . .

. . .

Derivative - A Clinical Trial

[0267] The PPAR-mediated disease is an inflammatory, proliferative or degenerative skin disease such as psoriasis, keratitis, hidradenitis, ichthyosis, **acne**, rosacea, verrucae and other HPV infections, atopic dermatitis, allergic dennatitis, chemical (irritant) dermatitis, seborrheic dermatitis, solar dermatitis, acute and chronic eczema, seborrheic keratosis,. . .

universalis)

Acne (all forms, including a. vulgaris, a. rosacea, a. inversa, cystic **acne**).

ACCESSION NUMBER: 2002076177 PCTFULL ED 20021011 EW 200240
TITLE (ENGLISH): DESIGN AND SYNTHESIS OF OPTIMIZED LIGANDS FOR PPAR
TITLE (FRENCH): CONCEPTION ET SYNTHESE DE LIGANDS OPTIMISES POUR PPAR
INVENTOR(S): PERSHADSINGH, Harrihar, Ajodhya; AVERY, Mitchell, Allen

PATENT ASSIGNEE(S): BETHESDA PHARMACEUTICALS, INC., for all designates States except US; PERSHADSINGH, Harrihar, Ajodhya, for US only; AVERY, Mitchell, Allen, for US only
AGENT: JOHNSTON, Madeline, I.
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2002076177	A2	20021003
DESIGNATED STATES	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG		
APPLICATION INFO.:	WO 2002-US9287	A	20020325
PRIORITY INFO.:	US 2001-60/278,097		20010323
	US 2001-60/283,774		20010413

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DETD Anti-**Acne** Actives.

Examples of useful anti-**acne** actives include the keratolytics such as salicylic acid (o-hydroxybenzoic acid), derivatives of salicylic acid such as 5-octanoyl salicylic acid and 4-methoxylsalicylic acid, and resorcinol; **retinoids** such as **retinoic** acid and its derivatives (e.g., cis and trans); sulfur-containing D and L amino acids and their derivatives and salts, particularly their N-acetyl. . .

Examples of antiwrinkle and anti-skin atrophy actives include **retinoic** acid and its derivatives (e.g., cis and trans); **retinol**; retinal; retinyl esters (e.g., retinyl acetate, retinyl palmitate, and retinyl proprionate); vitamine B3 compounds (such as niacinamide and nicotinic acid), salicylic acid. . . (available from Laboratories Serobiologiques); formononetin; forsythia fruit extract; gallic acid esters; gamma butyric acid; GATULINE RC (available from Gattlefosse, located in Priest, France); **genistein**; genisteine; genistic acid; gingko bilboa extracts; ginseng extracts; ginsenoside (RO, R6-1, R6-2,R6-3, RC, RD, RE, RF, RF-2, RG-1, RG-2); gluco pyranosyl-I-ascorbate;. . .

. . .

phosphate, MELAWHITE (available from Pentapharm), morus alba extract, mulberry root extract, niacinamide, 5-octanoyl salicylic acid, parsley extract, phellinus linteus extract, pyrogallol derivatives, **retinoic** acid, **retinol**, retinyl esters (acetate, propionate, palmitate, linoleate), 2, 4 resorcinol derivatives, 3, 5 resorcinol derivatives, rose fruit extract, salicylic acid, Song-Yi extract, 3,. .

.

. . .
the group
consisting of salicylic acid, benzoyl peroxide, 3-hydroxy benzoic acid, glycolic acid, lactic
acid, 4-hydroxy benzoic acid, acetyl salicylic acid, niacinamide, cis-**retinoic** acid, trans-
retinoic acid, **retinol**, retinyl palinitate,
2-hydroxybutanoic acid, 2-hydroxypentanoic acid,
2-hydroxyhexanoic acid, cis-**retinoic** acid, trans-
retinoic acid, **retinol**, phytic acid, N-acetyl-
L-cysteine, lipoic acid, azelaic acid, arachidonic acid,
benzoylperoxide, tetracycline,
ibuprofen, naproxen, hydrocortisone, acetominophen, resorcinol,
phenoxyethanol,
phenoxypropanol, phenoxyisopropanol, 2,4,4'-trichloro-2'-hydroxy
diphenyl ether,. . .

CLMEN. . . said cleansing article further
comprises a safe and effective amount of one or more active ingredients
selected from the group
consisting of anti-**acne** actives, anti-wrinkle and anti-skin
actives, skin barrier repair actives, non-
steroidal cosmetic soothing actives, non-stearoidal anti-inflammatory
actives, topical anesthetics,
artificial tanning agents. . .
. . .
group
consisting of salicylic acid, benzoyl peroxide, 3-hydroxy benzoic acid, glycolic acid, lactic acid, 4-
hydroxy benzoic acid, acetyl salicylic acid, niacinamide, cis-
retinoic acid, trans-**retinoic** acid, **retinol**,
retinyl palmitate, 2-hydroxybutanoic acid, 2-hydroxypentanoic acid,
2-hydroxyhexanoic acid, cis-
retinoic acid, trans-**retinoic** acid, **retinol**
, phytic acid, N-acetyl-L-eysteine, lipoic acid, azelaic acid,
arachidonic acid, benzoylperoxide, tetracycline, ibuprofen, naproxen,
hydrocortisone,
acetominophen, resorcinol, phenoxyethanol, phenoxypropanol,
phenoxyisopropanol, 2,4,4'-tr ichloro-
2'-hydroxy diphenyl. . .

ACCESSION NUMBER:	1999013861 PCTFULL ED 20020515
TITLE (ENGLISH):	CLEANSING AND CONDITIONING ARTICLE FOR SKIN OR HAIR
TITLE (FRENCH):	ARTICLE NETTOYANT ET REVITALISANT POUR LA PEAU OU LES CHEVEUX
INVENTOR(S):	McATEE, David, Michael; NISSING, Nicholas, James; HASENOEHRL, Erik, John; CABELL, David, William
PATENT ASSIGNEE(S):	THE PROCTER & GAMBLE COMPANY
LANGUAGE OF PUBL.:	English
DOCUMENT TYPE:	Patent
PATENT INFORMATION:	

NUMBER	KIND	DATE
WO 9913861	A1	19990325

DESIGNATED STATES	AL AM AT AT AU AZ BA BB BG BR BY CA CH CN CU CZ CZ DE DE DK DK EE EE ES FI FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.:	WO 1998-IB1362	A	19980831
PRIORITY INFO.:	US 1997-60/058,608		19970912
	US 1998-60/072,440		19980126
	US 1998-60/085,495		19980514

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DETD **Genistein** is a tyrosine kinase inhibitor and is under investigation for the
I 0 treatment of diseases involving cellular proliferation. **Genistein** is practically insoluble
in water.

Tretinoin is a **retinoic** acid that is being investigated as an anticancer
agent. Tretinoin is practically insoluble in water.

As mentioned above, additional preferred drugs for inclusion in polymeric delivery systems include camptothecin, amphoterecin, nystatin, tretinoin,
genistein, and curcumin. Camptothecin is also an insoluble drug in aqueous solutions.

Tretinoin is a **retinoic** acid marketed as Retin-A (Registered in the name
of McNeil Pharmaceutical Ltd.) for the treatment of **acne**. This agent increases
membrane permeability in certain cell particles; the lysosomes, thereby releasing certain
enzymes which may inhibit keratin formation and mucous metaplasia. **Retinoic** acid is
also a cell-differentiating agent and is being explored as an anticancer agent.

Genistein is a tyrosine kinase inhibitor which leads to the inhibition of
cell activation. Tyrosine kinases are signaling enzymes that promote cell surface
receptors to transmit activation signals into the cell. Therefore, **genistein** may be used
as an anti-inflammatory, anti-proliferative, anti-angiogenic or anticancer agent. Since
this agent may detrimentally affect all cells systemically, localized application. . .
. . .
and Tretinoin were a kind gift from Dr. K. Wasan (University of B.C., Vancouver, B.C., Canada). All other hydrophobic drugs, including curcurnin,
genistein, tretinoin, nystatin, amphoterecin, and camptothecin were obtained from
Sigma Chemicals (St. Louis, MO). Methotrexate and colchicine (Sigma Chemicals)
were used as examples. . .

EXAMPLE 7
ASSESSMENT OF DRUG-DEPENDENT SOLIDIFICATION
Compositions containing 10% w/w drugs (methotrexate, colchicine, curcumin, **genistein**, tretinoin, nystatin, amphoterecin, camptothecin or paclitaxel) were
manufactured using a 40:60 (TB:MEPEG'350) composition. Fifteen milligrams ofeach
composition were placed in a 20. . .
. . .
therefore, failed to solidify in water at 37'C (Figure 6). However, paste compositions containing the highly hydrophobic and water
insoluble drugs curcurnin, **genistein**, tretinoin, nystatin, amphoterecin, camptothecin or

paclitaxel stayed intact for over 4 minutes under stirring, which indicated that these
compositions had solidified. The. . .

Curcumin, **genistein**, tretinoin, nystatin, amphoterecin, camptothecin,
and paclitaxel are described in The Merck Index as being insoluble in water. Studies by
the present inventors. . .

. . .

100 0.038±0.01 8
492nm Absorbance of controls = 0.47±0.05
EXAMPLE 9
DETERMINATION OF IN'ViTRo DRUG RELEASE
Formulations containing I 0% w/w drugs (methotrexate, colchicine, curcumin, **genistein**, tretinoin, nystatin, amphoterecin, camptothecin or paclitaxel) were
manufactured using a 40:60 (TB:MePEG-')50)1 composition. Formulations containing
2.5%, 5%, 10%, and 15% paclitaxel were. . .

Genistein, which has a very low water solubility (approximately I
Vtg/mL), was released the fastest of all the hydrophobic drugs. However, only. . .

CLMEN. . . system of claim I wherein said
hydrophobic drug is selected from the group consisting of amphotericin, anthralin,
beclornethasone, betarnethasone, camptothecin, curcumin, dexamethasone, indomethacin,
genistein, lidocaine, insulin, nystatin, paclitaxel.
tetracycline, tretinoin, cromoglycate,
levobunolol, and terbinafine.

. . .

drug delivery system of claim 20 wherein said
hydrophobic drug is selected from the group consisting of paclitaxel, camptothecin,
amphoterecin, nystatin, tretinoin, **genistein**, and curcurnin.

ACCESSION NUMBER:	1999021908 PCTFULL ED 20020515
TITLE (ENGLISH):	POLYMERIC SYSTEMS FOR DRUG DELIVERY AND USES THEREOF
TITLE (FRENCH):	SYSTEMES POLYMERES DE LIBERATION DE MEDICAMENTS ET UTILISATION DE CES SYSTEMES
INVENTOR(S):	JACKSON, John; ZHANG, Xichen; BURT, Helen, M.
PATENT ASSIGNEE(S):	ANGIOTECH PHARMACEUTICALS, INC.; UNIVERSITY OF BRITISH COLUMBIA; JACKSON, John; ZHANG, Xichen; BURT, Helen, M.
LANGUAGE OF PUBL.:	English
DOCUMENT TYPE:	Patent
PATENT INFORMATION:	

NUMBER	KIND	DATE
WO 9921908	A1	19990506

DESIGNATED STATES	AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:	WO 1998-CA994 A 19981029
PRIORITY INFO.:	US 1997-60/063,721 19971029
	US 1998-60/076,842 19980304
	US 1998-09/181,582 19981028

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DETD . . . are not limited to, dry skin, ichthyosis, paimar and plantar hyperkeratoses, dandruff, lichen simplex chronicus, Dariers disease, keratoses, lentigines, age spots, melasmas, blemished skin, **acne**, psoriasis, eczema, pruritis, inflammatory dermatoses, striae distensae (i.e. stretch marks), warts and calluses.

. . .

with other cosmetic and pharmaceutical actives and excipients. Suitable other cosmetic and pharmaceutical agents include, but are not limited to, antifungals, vitamins, sunscreens, **retinoids**, antiallergenic agents, depigmenting agents, anti-inflammatory agents, anesthetics, surfactants, moisturizers, exfolients, stabilizers, preservatives, antiseptics, thickeners lubricants, humectants, chelating agents and skin penetration enhancers, as well as. . .

. . .

to about 50 wt.%, and most preferably about 5 wt.-0o to about 20 wt.% of the oxa acids co-formulated with (i) **retinoids** such as **retinol**, **retinoic** acid, retinyl palmitate, retinyl propionate, retinyl acetate, isotretinoin as well as synthetic **retinoid** mimics; (ii) hormonal compounds such as estriol, estradiol, estrone or conjugated estrogens; (iii)
20
alpha-hydroxyacids or polyhydroxy alpha-hydroxy acid such as glycolic acid, lactic acid,. . .

. . .

the oxa acids in combination with antioxidants with phenolic hydroxy functions such as gallic acid derivataives (e.g. propyl galiate), bio-flavonoids (e.g. quercetin, rutin,
25
daidzein, **genistein**), ferrulic acid derivatives (e.g.

EXAMPLE 5
Cream for **Acne**, Skin Blemishes and Age Spots
This example illustrates a face cream than can be used to treat **acne**, skin blemishes and age spots.

wt.%
Phase A
oleic acid 1.0
stearic acid 17.0
polyoxyethylene (20 propylene glycol monostrearate) 10.0
retinol 0.1
Phase B
glycerine 5.0
2-pyrollidone carboxylic acid 5.0
3,6,9-trioxadecanoic acid 7.5
3,6-dioxaheptanoic acid amide 2.5
lactic acid 3.0
demineralized water to 100.0
ammonium hydroxide to pH 4.2
All. . .

CLMEN 15 The composition of claim 1, further comprising at least one active selected from the group

consisting of antifungals, vitamins, sunscreens, **retinoids**, antiallergenic agents, depigmenting agents, anti-inflammatory agents, anesthetics, surfactants, moisturizers, exfolients, emulsifiers, stabilizers, 39 preservatives, antisepticsf emollients, thickeners, lubricants, humectants, chelating agents, fragrances, colorants and skin penetration. . .

. . .

the group consisting of dry skin, ichthyosis, palmar and plantar 48 hyperkeratoses, dandruff, lichen simplex chronicus, Dariers disease, keratoses, lentigines, age spots, melasmas, blemished skin, **acne**, psoriasis, eczema, pruritis, inflammatory dermatoses, striae distensae, warts, calluses, signs of dermatological aging, skin wrinkles, fine wrinkles around the mouth area, irregular pigmentation, sallowness,. . .

. . .

The method of claim 35, wherein said composition further comprises at least one active selected from the group consisting of antifungals, vitamins, sunscreens, **retinoids**, antiallergenic agents, depigmenting agents, anti-inflammatory agents, anesthetics, surfactants, moisturizers, exfolients, emulsifiers, stabilizers, preservatives, antiseptics, emollients, thickeners, lubricants, humectants, chelating agents, fragrances, colorants and skin penetration enhancers. 49

.. . .

ACCESSION NUMBER:	1997046231 PCTFULL ED 20020514
TITLE (ENGLISH):	OXA ACIDS AND RELATED COMPOUNDS FOR TREATING SKIN CONDITIONS
TITLE (FRENCH):	ACIDES OXA ET COMPOSES APPARENTES UTILISES DANS LE TRAITEMENT D'ETATS DERMATOLOGIQUES
INVENTOR(S):	PTCHELINTSEV, Dmitri; SCANCARELLA, Neil; KALAFSKY, Robert
PATENT ASSIGNEE(S):	AVON PRODUCTS, INC.
LANGUAGE OF PUBL.:	English
DOCUMENT TYPE:	Patent
PATENT INFORMATION:	

NUMBER	KIND	DATE
WO 9746231	A1	19971211

DESIGNATED STATES	BR CA CN JP MX AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.:	WO 1997-US9281 A 19970602
PRIORITY INFO.:	US 1996-8/658,089 19960604

L48 ANSWER 29 OF 45 PCTFULL COPYRIGHT 2002 Univentio

DETD . . . are not limited to, dry skin, ichthyosis, palmar and plantar hyperkeratoses, 8 dandruff, lichen simplex chronicus, Dariers disease, keratoses, lentigines, age spots, melasmas, blemished skin, **acne**, psoriasis, eczema, pruritis, inflammatory dermatoses, striae distensae (i.e. stretch marks), warts and calluses.

. . .

combinations with other cosmetic and pharmaceutical actives and excipients. Suitable other

cosmetic and pharmaceutical agents include, but are not limited tof antifungals, vitaminsf sunscreensf **retinoids**, antiallergenic agents, depigmenting agents, 18
anti-inflammatory agents, anesthetics, surfactants, moisturizers, exfolients, stabilizers, preservatives, antiseptics, thickeners lubricants, humectants, chelating agents and skin penetration enhancers, as well as. . .
. . .
preferably from about 1 to about 50%, and most preferably about 5 to about 20% of the oxa diacids co-formulated with (i) **retinoids** such as **retinol**, **retinoic** acid, retinyl palmitate, retinyl propionate, retinyl acetate, isotretinoin as well as synthetic **retinoid** mimics; (ii) hormonal compounds such as estriol, estradiol, estrone or conjugated estrogens; (iii) alpha-hydroxyacids or polyhydroxy alpha-hydroxy acid such as glycolic acid, lactic acid,. . .
. . .
oxa diacids in combination with antioxidants with phenolic hydroxy functions such as gallic acid derivataives (e.g. propyl gallate), bio-flavonoids (e.g. quercetin, rutin, daidzein, **genistein**), ferrulic acid derivatives (e,g, ethyl ferrulate, sodium ferrulate), 6-hydroxy-2,5,7,tetra-, methy1chroman carboxylic acid. The compositions may also contain effective concentrations of water soluble antioxidants such. . .

EXAMPLE 6
Cream for **Acne**, Skin Blemishes and Age Spots
This example illustrates a face cream than can be used to treat **acne**, skin blemishes and age spots.

37
W/W%
Phase A
oleic acid 110
stearic acid 1740
polyoxyethylene (20 propylene glycol monostrearate) 10*0
retinol O'l
Phase B
glycerine 5,0
2-pyrollidone carboxylic acid 5,0
3,6,9-trioxaundecanedioic acid 7,5
3,f6,f9tl2-tetraoxatetradecanedioic acid 2,5
lactic acid 3,0
demineralized water to 100,0
ammonium hydroxide to pH 4.2
All numbers. . .

CLMEN 15 The composition of claim 1, further comprising at least one active selected from the group consisting of antifungals, vitamins, sunscreens, **retinoids**, antiallergenic agents, depigmenting agents, anti-inflammatory agents, anesthetics, surfactants, moisturizers, exfolients, emulsifiers, stabilizers, preservatives, antiseptics, emollients, thickeners, lubricants, humectants, chelating agents, fragrances, colorants and skin penetration. . .

. . .
The method of claim 29, wherein said composition further comprises at least one active selected from the group consisting of antifungals, vitamins, sunscreens, **retinoids**, antiallergenic agents, depigmenting agents, anti-inflammatory agents, anesthetics, surfactants, moisturizers, exfolients, emulsifiers, stabilizers, preservatives, antiseptics, emollients, thickeners, lubricants, humectants, chelating agents, fragrances, colorants and skin penetration enhancers.

ACCESSION NUMBER: 1997039726 PCTFULL ED 20020514
TITLE (ENGLISH): OXA DIACIDS AND RELATED COMPOUNDS FOR TREATING SKIN CONDITIONS
TITLE (FRENCH): DIACIDE OXA ET COMPOSES VOISINS POUR TRAITER LES PROBLEMES DE PEAU
INVENTOR(S): PTCHELINTSEV, Dmitri; SCANCARELLA, Neil; KALAFSKY, Robert
PATENT ASSIGNEE(S): AVON PRODUCTS, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9739726	A1	19971030

DESIGNATED STATES: BR CA CN JP MX AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1997-US6973 A 19970425
PRIORITY INFO.: US 1996-8/636,540 19960425

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DETD TABLE -1
FIRST COMPOSITION SECOND COMPOSITION
Cleanser Moisturizer
Cleanser Anti-**acne** preparation
Cleanser Moisturizer
Cleanser Facial Foundation
Moisturizer Toner
Cleanser Skin Lightener
Self-Tanner Cleanser
Cleanser Sunscreen
Skin Lightener Sunscreen
Sunscreen Anti-wrinkle Cream
Moisturizer Sunscreen
It is to be understood that this. . .

Suitable **retinoids** are **retinol**, **retinoic** acid or the CI@C20 esters of **retinol** and **retinoic** acid. Illustrative ceramides are Ceramide 1, Ceramide 2, Ceramide 3 and Ceramide 6.

Pseudoceramides may also be useful. Levels of **retinoids** and ceramides may suitably range from O..00001 to 2%. preferably from 0.0001 to 0.1% by weight.

Anti-**acne** preparations will usually include an active selected from the group consisting of benzoyl peroxide, an alpha-hydroxycarboxylic acid, salicylic acid, **retinoids** and their derivatives. Amounts of these materials may suitably range from 0.1 to 30% by weight of the composition.

TABLE IV

CLEANSER
COMPONENT WEIGHT %
Glycerin 1.50
Polyoxyethylene 1.50
hydrogenated castor oil
Sorbitan stearate 1.00
Squalane 10.00
Dipropylene glycol 5.00
Genistein 0.10
water qs 10 0.00
TABLE V
SKIN-LIGHTENER
COMPONENT WEIGHT
Polysorbate 80 1.00
Ethyl alcohol 3.00
Polyethylene glycol-600 5.00
Citric acid 0.03
Sodium citrate 0.20
0-Ethyltetraacet@71glucosaniine. 0.10
Methylparaben 0.10
.Fragrance qs
Water qs. . .

CLMEN. . . independently include an active material selected from the group consisting of alpha-hydroxycarboxylic acid or salts thereof, beta-hydroxycarboxylic acids or salts thereof, sunscreens, **retinoids**, ceramides, surfactants, self-tanners and mixtures thereof.

ACCESSION NUMBER:	1996037420 PCTFULL ED 20020514
TITLE (ENGLISH):	TREATMENT REGIME FOR SKIN
TITLE (FRENCH):	CURE DE SOINS CUTANES
INVENTOR(S):	SUARES, Alan, Joseph; NETTESHEIM, Susan; INDURSKY, Michael; BERTOLINI, Peter
PATENT ASSIGNEE(S):	UNILEVER PLC; UNILEVER N.V.
LANGUAGE OF PUBL.:	English
DOCUMENT TYPE:	Patent
PATENT INFORMATION:	

NUMBER	KIND	DATE
WO 9637420	A1	19961128

DESIGNATED STATES	AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1996-EP2274	A	19960524
PRIORITY INFO.:	US 1995-8/451,940		19950526
	US 1996-60/005,188		19960513

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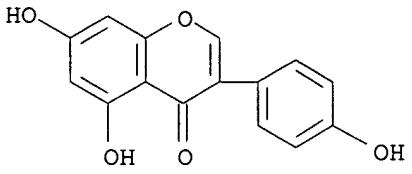
RN 446-72-0 REGISTRY
CN 4H-1-Benzopyran-4-one, 5,7-dihydroxy-3-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Genistein (6CI)**
CN Isoflavone, 4',5,7-trihydroxy- (8CI)
OTHER NAMES:
CN 4',5,7-Trihydroxyisoflavone
CN 5,7,4'-Trihydroxyisoflavone
CN Baichanin A
CN C.I. 75610
CN Genisteol
CN Genisterin
CN NPI 031L
CN Prunetol
CN SIPI 807-1
CN Sophoricol
FS 3D CONCORD
MF C15 H10 O5
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, HODOC*, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2814 REFERENCES IN FILE CA (1962 TO DATE)
53 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2836 REFERENCES IN FILE CAPLUS (1962 TO DATE)
34 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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